FUNCTIONAL STATE OF ANTIOXIDANT SYSTEM UNDER INFLUENCE OF RADIATION LOW DOSES

I. V. Voltchek, E. V. Kostyushov, L. L. Goncharova,
I. S. Izyumtsev, V. A. Dyachek, A. A. Tyaptin,
I. N. Popov, S. A. Kalikanov, L. V. Filyov

Department of Extreme Medicine,
St. Petersburg Institute of Advanced Medical Studies,
St. Petersburg, Russia

ABSTRACT

The functional state of blood antioxidant system (AOS) was studied at liquidators of Chernobyl AES crash 4-5 years ago irradiation (200-250 mSv). The increasing SH/SS ratio in protein and non-protein thioldisulfide system, the prevailing of ascorbic acid oxiforms in plasma, changes activity of catalase, glutathionreductase and superoxidedismutase, rising of the intensity of peroxide lipid oxidation and nucleotides degradation have been revealed. Thus, the adaptational failure of the AOS may be regarded as one of the leading links in low dose irradiation injuring effect.

INTRODUCTION

It is now evident that one of the most common manifestations of the effect of stressor agents on man's organism is the intensification of free-radical oxidation processes. Obviosly, this fact is to be regarded as a side effect of the growing intensity of biochemical reactions in response to the action of extreme factors, including radiation through neuro-endocrine regulation mechanisms [1]. As known, these processes are capable of excersizing multiplan injuring effect on living cell.

The manifestation of the injuring effect of free radicals and peroxide compounds is hindered by the complex multicomponent antioxidant system (AOS) providing binding and modification of radicals, the prevention of peroxides formation or their destruction. In its composition are included bioantioxidants of different nature and antiperoxide enzymes [2, 3]. So, pro- and antioxidant systems exist in dynamic equilibrium and provide in their interaction the adaptive reactions in response to the effect of extreme factors, ensuring radioresistance of organism [4].

MATERIALS AND METHODS

Complex clinical examination employing modern functional and biochemical methods was conducted with 35 men-liquidators of the consequences of Chernobyl AES crash 4-5 years ago radiation influence in doses 200-250 mSv per 1-2 months. The observed patients were suffered from different internal diseases (neurocirculatory asthenia, hypertensive and

ischemic heart diseases, stomach and duodenum ulcers, chronic gastroduodenitis) which have been revealed after their work in Chernobyl. The control group consists of 104 healthy donors. We studied contents of sulfhydril (SH) and disulfide (SS) groups in whole blood [5], concentrations of ascorbic acid (AA) and its oxiforms (OF) in plasma [6]. Activity of superoxidedismutase (SOD), catalase and glutathionreductase (GR) was determined [7]. Intensity of peroxide lipid oxidation was estimated by accumulation of malone dialdehyde (MDA) in whole blood [8]. Valuing of lymphocyte products of nucleotides degradation (PND) was executed by the spectrofluorimetrik method [9].

RESULTS

As the analysis of data obtained has demonstrated changes were observed in the non-enzymatic link of the AOS in low dose irradiated patients (Table).

TABLE Values of AOS in low dose irradiated patients

PROOFS	CONTROL GROUP	PATIENTS
Protein		
SH (mM/l)	13.00 ± 0.20	12.30 ± 0.20 *
SS (mM/l)	4.80 ± 0.10	3.79 ± 0.18 **
SH/SS	2.70 ± 0.20	3.81 ± 0.22 *
Non-protein		
SH (mM/l)	1.14 ± 0.01	1.35 ± 0.10 *
SS (mM/l)	0.41 ± 0.01	0.42 ± 0.10
SH/SS	2.80 ± 0.30	3.69 ± 0.29 *
AA/OF	0.84 ± 0.13	0.24 ± 0.05 *
Catalase (mKat/g)	601.7 ± 14.9	657.3 ± 34.9
GR (nKat/g)	18.5 ± 0.6	19.8 ± 1.2
SOD (% of inhib.)	29.6 ± 0.9	17.2 ± 1.6 *
MDA (μ M/l)	76.8 ± 5.1	101.8 ± 2.5 *
PND (%)	50.0 ± 8.5	70.7 ± 1.5 *

* - differences with a control group are significant (* - $p<0.05$, ** - $p<0.01$) by Fisher test

In particular, the significant disorders were observed in thioldisulfide system which displayed by increasing of SH/SS ratio both in protein and non-protein fractions of the solid blood. And if in protein part it was connected with the reducing value of SS-groups then in non-protein part it was due to significant increasing value of SH-groups.

At the same time the functional state of ascorbic redox system was characterized by the great prevailing of its oxiforms in plasma.

Changes of enzymatic function were exclusively individual: the activity of catalase and GR more often has

been increased than decreased but overall there weren't differences between the enzymatic activity of low dose irradiated patients in comparison with a control group. At the same time SOD was depressed in all observations.

On the background of data obtained the level of MDA and PND were significantly rised.

DISCUSSION

The increasing of non-protein SH-groups and enzymatic activity may testify the hormetic influence of low dose irradiation on the nonspecific resistance in the process of adaptation. From the one side, unproportional decreasing of protein SS- (to a considerable extent) and SH- groups (to a smaller extent) may be limited by structural protein alteration which are accompanied by changes of correlation between camouflage and accessible for determination protein thiol and disulfide groups. From the other side, the rising of protein SH/SS ratio may be regarded as the protective reaction at the more low adaptational level in the conditions of the oxidizing agents excess which is realized at non-protein group expence.

Even under conditions of AOS adaptative activation there aren't abilities to prevent the increasing of peroxide lipid oxidation, DNA degradation and reducing of ascorbic acid oxiforms. So, our data give reason to suggest the significant role of antioxydant insufficiency in the launching mechanisms of disease in low dose irradiation.

At the level of cell metabolism it is manifested in peroxidation reactions, whose biochemical substrate are practically all biomolekules, which leads to injuring their nativity. Its consequence is disturbance of biological activity, synthesis, transport and inactivation of enzymes, hormones, vitamins, mediators and other substances, as well as change of receptivity, membrane permeability, energetic deficit, disturbance of hemoglobin transport of oxigen and its utilisation by tissue. This leads to proliferation and differentiation disorders, disintegration of humoral and cellular defence mechanisms, including the immune [10].

In its turn, the result of the changes indicated is disturbance of circulatory homeostasis system, vessel reactivity and microcirculation, heart activity, as well as disorder of pulmonary gas exchange leading to hypoxia of tissues and organs. Subsequent hemocirculatory disturbances together with tissue and cell hypoxia lead to functional and morphological modifications in organs and lifesecuring systems and to development of various organ's pathology in low dose irradiated persons.

CONCLUSIONS

For our opinion, the adaptational failure of the antioxidant system may be regarded as one of the leading links in pathogenesis of damage by radiation low doses.

The methods employed can be recommended for the estimation of radiation danger, standartization and elaboration of the directions for radioprotection. Achived results enable us to propose a pathogenetically founded metabolic therapy of injuries induced by low dose radiation with the employment of antioxidants.

REFERENCES

1. Kuzin, A.M., 1986, Structural metabolic theory in radiobiology, Moscow, 284 p.

2. Sokolovsky, V.V., 1988, Thiol antioxidants in molecular mechanisms of organism nonspecific reaction on the action of environment extreme factors, Quest. Med. Chem., 34, 6, pp. 2-11.

3. Kostyushov, E.V., 1984, The role of thioldisulfide and ascorbic redox systems in late toxicosis of the pregnant, Minsk, pp. 1-20.

4. Burlakova, E.B., Ivanenko, G.Ph., Shishkina, L.N., 1985, A contribution of antioxidants and endogenous thiols to ensuring radioresistance of organism, Proc. Acad. Sci. USSR, Ser.: Biol., 4, pp. 588-593.

5. Sokolovsky, V.V., Belozyorova, L.A., Ogurtsova, R.E., 1977, Method of quantative analysis of disulfide groups in blood by reverse amperometric titration, Lab. work, 1, pp. 26-27.

6. Sokolovsky, V.V., Lebedeva, L.V., Lielup, T.B., 1974, Separate determination of ascorbic, dehydroascorbic and diketogulonic acids content in serum, Lab work, 3, pp. 160-162.

7. Beutler, E., 1975, Red cell metabolism: a manual of biochemical methods, Sec. Edd. - N.Y.

8. Andreeva, L.I., Kozhemyakin, L.A., Kishkun, A.A., 1988, A modified thiobarbituric acid test for measuring lipid peroxidation products, Lab. work, 11, pp. 41-43.

9. Ivannik, B.P., Sin'Kova, R.V., Konov, A.V., Ryabchenko, N.I., 1986, Chromatin endonucleolysis in thymocytes of irradiated and nonirradiated rats, Radiobiol., 26 , 2, pp. 162-166.

10. Voltchek, I.V., Filyov, L.V., Kostyushov, E.V., and co-workers, 1991, About the disorders of mononuclear antiviral resistance under influence of low dose radiation, Human immune status and radiation, All-Union Sci. Conf. (Gomel), Moscow, pp. 130-131.