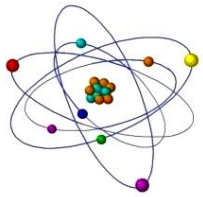
ALTERATION OF PATIENTS' BLOOD TOTAL ANTIOXIDANT ACTIVITY DURING RADIOTHERAPY



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ABSTRACT: *This article presents the results of studies that examined the general antiradical status (TAA) of the body as a potential biomarker of the effects of radiation exposure. Thirty patients (60-70 years old) with squamous cell carcinoma of the larynx participated in the study. Every patient underwent fractional radiation therapy. Irradiation was performed on a linear accelerator in 2 gray/fraction mode, with a total dose of 70 gray given by a radical program. The examination of blood TAA was performed before the treatment (I) in the middle of treatment where the patient had received half of the total acceptable treatment dose (II) and after the radiation (III). In our study it was found that the TAA of blood increases linearly within the error, which indicates the activation of the body's antioxidant defense systems with the aim to neutralize the radicals generated by ionizing radiation.*

The results of our investigation support the fact that the non-enzymatic antiradical system plays an important role in the prevention of radiation damage during ionizing radiation exposure.

Key words: antioxidant activity, blood, irradiation

INTRODUCTION

Major advances in medical and radiation therapy have contributed to a growing population of cancer survivors. However, survivors have experienced adverse effects of radiotherapy [1,2], ICRP recommends the search for new highly effective, and inexpensive biomarkers of the individual risk for tissue reactions and strategies to prevent/mitigate tissue effects after exposure [3], which is considered to be a modern priority in radiation biomedicine [4]. Modern approaches to the search for absorbed dose (dose marker), radio-induced shifting effect, and marker of susceptibility in the conditions of the fractional partial body irradiation are concentrated on complex - genetic, cytogenetic, metabolic characteristics [5,6]. Among biodosimetry markers of radiation exposure, special attention is paid to redox status imbalance biomarkers [7, 8].

Ionizing radiation's hazardous impacts on living tissue are mediated by the generation production of reactive oxygen species (ROS) and oxidative stress mechanisms. ROS (hydroxyl radical, superoxide anion, and hydroperoxyl radicals) are generated after the irradiation, in the process of radiolysis of water [7, 8], followed by a chronic inflammatory response [9], accumulation of free radicals, and ROS, shift the redox equilibrium of the cell towards the oxidized state and development of an imbalance between pro-oxidative and antioxidative reactions, depletion of antioxidant activity together with an occurrence of negative consequences in metabolism [10].

Specialized enzymatic and non-enzymatic antioxidant systems participate in preventing the high production of free radicals in the eukaryotic organisms' cells. An especially important role in these mechanisms plays a nonenzymatic antioxidant system (total low molecular weight antioxidants (ascorbic acid, bilirubin, estrogens, biogenic amines (dopamine, histamine, serotonin, melatonin and amino acid, tryptophan), etc.)), known as a total antioxidant activity (TAA) of the blood plasma.

This article presents the results of studies that examined the general antiradical status (TAA) of the body as a potential biomarker of the effects of radiation exposure.

MATERIAL AND METHODS

Thirty patients (60-70 years old) with squamous cell carcinoma of the larynx participated in the study. Every patient underwent fractional radiation therapy. Irradiation was performed on a linear accelerator in 2 gray/fraction mode, with a total dose of 70 gray given by a radical program. Patients were irradiated on the basis of the Live Hospital-Radiation Center with the device "Electra Synergy Platform". The study protocol was prooved by the Ethical Committee of Tbilisi State Medical University. Patients were informed about their participation in the study and signed written consent.
Postoperative patients were mostly irradiated with 66 grays in 33 fractions with a daily dose of 2 grays. Nonoperative patients were mostly irradiated with 70 grays in 35 fractions - with a daily dose of 2 grays. The examination TAA of blood was performed before the treatment (I) in the middle of treatment where the patient had received half of the total acceptable treatment dose (II) and after the radiation (III).

TAA was determined in deproteinized blood plasma by using the 2.2-diphenyl-1-picrylhidrazyl (DPPH)-scavenging assay, which was adapted from a study conducted by Chrzczanowicz et al. [11]. Briefly, plasma samples (1 mL) were deproteinized by adding 3 mL of acetonitrile and centrifuging then for 10 min (4°C, 9500 ×g). A supernatant was immediately collected and 1 ml was transferred to a tube. Subsequently, 3 mL of DPPH was added, and the resultant absorbance was read at 515 nm. A calibration curve was built with the use of gallic acid, wherein the absorbance values were interpolated and the results were expressed as equivalents of gallic acid.

Statistical analysis

Each data point represents mean standard error on the mean (SEM) of at least six pacient per group. $P < 0.05$ was considered to represent a statistically significant difference.

RESULTS

Figure 1 shows the values of the blood TAA of healthy individuals (controls) and oncological patients before radiotherapy (I), after receiving half-dose (II), and after irradiation (III). According to the results of the study, the blood TAA of patients with laryngeal cancer was no different from the blood TAA of the same age (60-70 years old) healthy individuals. After receiving a half dose of radiotherapy, the TAA of the irradiated patients; blood increased almost 2 times compared to the initial values, and after the completion of the whole course, the level of the blood TAA increased by 5 times in comparison to initial values.

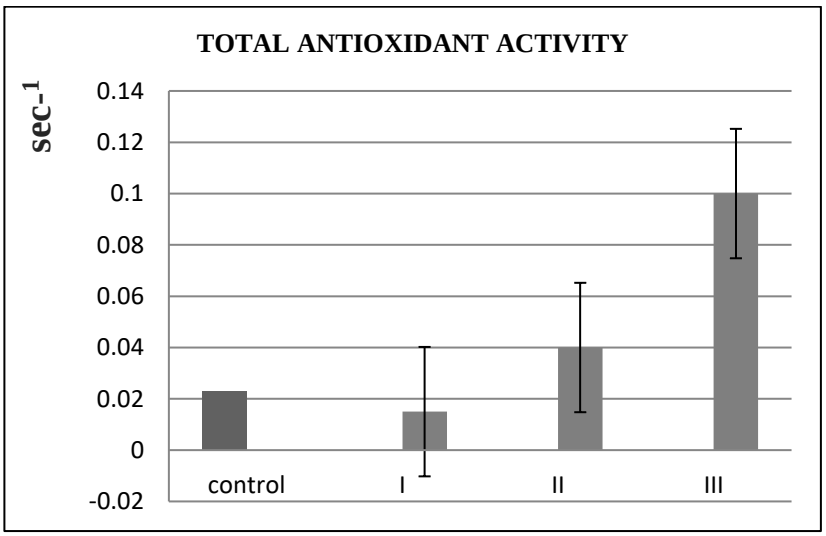

Figure 1. The blood TAA of healthy individuals (controls) and oncological patients before radiotherapy (I), after receiving half-dose (II), and after irradiation (III).

DISCUSSION

In response to the direct effect of ionizing radiation on cellular targets, in the result of radiolysis of water, as well as due to the compensatory response of the body to primary damage (increased activity of mitochondrial and microsomal electron transport systems) in tissues produced a huge amount of ROS, capable of damaging the cells and tissues of a living organism and leading it to death. The ability of cells in a living organism to prevent specific and non-specific oxidative damage is a key survival mechanism. Against the increased formation of ROS in the body, the enzymatic and the non-enzymatic antioxidant system, ensure the neutralization of free radicals [12, 13]. As shown by numerous studies, the antioxidant enzymatic system is rapidly depleted and cannot suppress an excess amount of ROSs formed during irradiation. In response to irradiation compensatory released high concentrations of low molecular weight antioxidants (ascorbic acid, biogenic amines, thiols, etc.) suppress oxidative stress [14, 15].

In our study it was found that the TAAof blood increases linearly within the error, which indicates the activation of the body's antioxidant defense systems with the aim to neutralize the radicals generated by ionizing radiation.

Small ROS-scavenging molecules present a metabolic route of tightly coordinated physiological processes ensuring the protection of cellular structures and macromolecules from ionizing radiation. The compensatory alterations of the TAA are a key mechanism of body resistance to ionizing radiation in radiated animals.

CONCLUSION

The results of our investigation support the fact that the non-enzymatic antiradical system plays an important role in the prevention of radiation damage during ionizing radiation exposure.

REFERENCES

1. Balazs I Bodai, Phillip Tuso, Breast Cancer Survivorship: A Comprehensive Review of Long-Term Medical Issues and Lifestyle Recommendations. The Permanente Journal/ Spring. 19(2), 48-79(2015).
2. Sarah C. Darby, at all, Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer, N Engl J Med. 368. 987-98 (2013).
3. ICRP publication 118: ICRP statement on tissue reactions and early and late effects of radiation in normal tissues and organs--threshold doses for tissue reactions in a radiation protection context. Ann ICRP.41(1-2), 1-322 (2012).
4. ICRP 2013: 2nd International Symposium on the System of Radiological Protection. Abu Dhabi. October 2013
5. Mary Sproull, Tamalee Kramp, Anita Tandle, Uma Shankavaram and Kevin Camphausen, Multivariate Analysis of Radiation Responsive Proteins to Predict Radiation Exposure in Total-Body Irradiation and Partial-Body Irradiation Models, RADIATION RESEARCH. 187, 251–258 (2017)/
6. C. Herate, L. Sabatier, Retrospective biodosimetry techniques: Focus on cytogenetics assays for individuals exposed to ionizing radiation, Mutation Research 783 (2020)
7. Moding, E. J. Kastan, M. B. and Kirsch, D. G. Strategies for optimizing the response of cancer and normal tissues to radiationev Drug Discov. 12(7), 526–542 (2013).
8. Amira Bryll, Wirginia Krzy´sciak, Anna Jurczak, Robert Chrzan, Anna Lizo ´n, Andrzej Urbanik. Changes in the Selected Antioxidant Defense Parameters in the Blood of Patients after High Resolution Computed Tomography. Int. J. Environ. Res. Public Health.16, 1476 (2019).
9. Zhao W, Diz DI, Robbins ME. Oxidative damage pathways in relation to normal tissue injury. Br. J. Radiol. 80, S23–S31 (2007)

10. Maryam Hazbavi, Mansoureh Zarei, Roghayeh Nazaralivand, Hojattollah Shahbazian, Mohsen Cheki. Protection from ionizing radiation-induced genotoxicity and apoptosis in rat bone marrow cells by HESA-A: a new herbal-marine compound. Journal of Bioenergetics and Biomembranes, (2019).

11. Chrzczanowicz, J. Gawron, A. Zwolinska, A. de Graft-Johnson,J. Krajewski, W. Krol, M. Markowski, J. Kostka, T. and Nowak, D. Simple method for determining human serum 2,2-diphenyl-1-picryl-hydrazyl (DPPH) radical scavenging activity - possible application in clinical studies on dietary antioxidants. Clinical Chemistry and Laboratory Medicine. 46, 342–349 (2008).

12. Kudryashov, Y. B. Radiation biophysics (ionizing radiations).Nova Science Publishers Inc (2008) ISNB 13:078-160021-280-2.

13. Karki, K. Pande, D. Negi, R. Khanna, R.S.and Khanna, H.D. An Assessment of Oxidative Damage and Non-Enzymatic Antioxidants Status Alteration in Relation to Disease Progression in Breast Diseases. Med. Sci. 4, 17, 1-11 (2016).

14. GvilavaI , G Ormotsadze , I Chkhikvishvili, M Giorgobiani, Nina V Kipiani , T Sanikidze RADIOPROTECTIVE ACTIVITY OF POLYMETOXY-LATED FLAVONOIDS OF CITRUS EXTRACT] Georgian Med News, . 2018 Dec;(285):119-124.

15. T. Sanikidze, S. Kalmakhelidze, I. Chkhikvishvili, E. Shekiladze, N. Ivanishvilli, E. Lomadze, M. Buleishvilii, D. Topuria, G. Ormotsadze. High-sensitive biomarkers of blood total antiradical activity in mice exposed to gamma–irradiation. International Journal of Innovative Research in Medical Science. 2021, 6(03),197 - 200