

CLINICAL RESEARCH

The effect of low dose ionizing radiation exposure on dynamic thiol-disulfide homeostasis and ischemia modified albumin levels: an observational study



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KEYWORDS

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Abstract

Background: The primary objective of this study was to investigate the effect of low dose ionizing radiation exposure on thiol/disulfide homeostasis and ischemia modified albumin levels. The secondary objective is to compare thiol/disulfide homeostasis and ischemia modified albumin levels among the personnel exposed to low dose ionizing radiation in anesthesia application areas, in and out of the operation room.

Methods: The study included a total of 90 volunteers aged between 18 and 65 years old, with 45 personnel working in a setting with potential for radiation exposure (Exposed Group) and 45 personnel in a setting without radiation exposure (Control Group). Their native thiol, total thiol, disulphide, albumine and IMA levels were measured. Exposed group included personnel who were exposed to radiation outside the operating room – Operation room (–) Group and inside the operating room – Operation room (+) Group.

Results: Albumin, native and total thiol levels were significantly lower in the participants exposed to radiation in the anesthesia application area; no statistically significant difference was found in terms of disulfide and ischemia modified albumin levels. In the Operation room (–) Group exposed to radiation, native thiol and total thiol values were significantly lower compared to the Operation room (+) Group.

Conclusion: Awareness of being in danger of oxidative stress should be established in personnel exposed to radiation in the anesthesia application area following low dose ionizing radiation exposure, and the necessary measures should be taken.

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PALAVRAS-CHAVE

Anestesia;
Albumina modificada por isquemia;
Radiação;
Tiol

Efeito da exposição à radiação ionizante de baixa dose na homeostase dinâmica de tiol-dissulfeto e níveis de albumina modificada por isquemia: estudo observacional**Resumo**

Justificativa: O objetivo principal do estudo foi investigar o efeito de exposição à radiação ionizante de baixa dose nos níveis de homeostase tiol/dissulfeto e de albumina modificada por isquemia. O objetivo secundário foi comparar os níveis de homeostase tiol/dissulfeto e albumina modificada por isquemia entre indivíduos expostos à radiação ionizante de baixa dose nas áreas de procedimentos anestésicos, dentro e fora da sala de cirurgia.

Método: O estudo incluiu um total de 90 voluntários com idades entre 18 e 65 anos, 45 profissionais que trabalhavam em ambiente de exposição potencial a radiação (Grupo Exposto) e 45 profissionais que trabalhavam em ambiente sem exposição à radiação (Grupo Controle). Foram medidos os níveis de tiol nativo, tiol total, dissulfeto, albumina e albumina modificada por isquemia. O Grupo Exposto era constituído por profissionais expostos a radiação fora da sala de cirurgia – Grupo sala de cirurgia (–) e dentro da sala de cirurgia – Grupo sala de cirurgia (+).

Resultados: Os níveis de albumina, tiol nativo e total foram significantemente mais baixos nos participantes expostos à radiação em área de realização de anestesia, e nenhuma diferença estatisticamente significante foi encontrada para os níveis de dissulfeto e albumina modificada por isquemia. No Grupo sala de cirurgia (–), os valores de tiol nativo e tiol total foram significantemente mais baixos quando comparados ao Grupo sala de cirurgia (+).

Conclusões: Os profissionais expostos à radiação em área de realização de anestesia devem ser conscientizados quanto ao perigo do estresse oxidativo após exposição à radiação ionizante de baixa dose e medidas cabíveis devem ser instituídas.

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Introduction

Epidemiological studies for people who have been involved in radiation accidents have provided basic health information about radiation exposure, and contributed to the development of guidelines for protection regarding radiation.¹ It is obvious that radiation exposure higher than 500 millisievert (mSv) can cause detrimental effects such as tissue damage, fatal effects and development of cancer.² Even in LDIR, which is just a few mSv similar to the levels of natural social background, there are concerns about the health risks of radiation exposure. Radiation specialists believe that consolidated evidences for the health risks of LDIR are necessary for decreasing public concern regarding being exposed in daily life.³ Especially, biological mechanical studies about radiation reaction in humans are strongly recommended by many international authorities regarding protection against radiation.⁴⁻⁶ In parallel with the recent technological developments, radiation exposure is increasing in healthcare staff working in diagnosis and treatment process.

Thiols are organic sulphur derivatives containing Sulphydryl Residues (–SH) in their active regions. Thiols easily react with oxygen containing free radicals to form disulfides. This is a defence mechanism against oxidative stress.⁷ An automated analysis quantitatively measuring serum native and total thiol, and disulfides has been recently described as a method to determine dynamic Thiol/Disulfide Homeostasis (TDH).⁸

Proteins are significant targets of oxidative attack. Albumin, which is the major plasma protein, has a number of

cation- and anion-binding sites and therefore it effectively inhibits oxidation reactions in plasma. It acts both as a freeradical scavenger and also as a chelator of transition metals, making this protein a potent antioxidant.⁹

There is a bonding location of transitional metal ions, including cobalt and copper, in the N-terminal region of albumin.¹⁰ Reactive oxygen radicals forming during ischemia change the N-terminal of albumin and irreversibly modify it to a dysfunctional form, known as Ischemia Modified Albumin (IMA). This causes a decrease in the ability of albumin to bind to nickel, cobalt and copper.¹¹

The primary objective of this study was to investigate the effect of LDIR exposure on TDH and IMA levels. The secondary objective was to compare TDH and IMA levels between the personnel exposed to LDIR in the anesthesia area out of the operation room and the personnel exposed to LDIR in the operation room.

Method

Selection of participants

The ethical approval of the study was received from Necmettin Erbakan University Medical Faculty Clinical Research Ethics Committee (Date: 25/05/209, n° 2019/1913). This study was conducted as a single center prospective observational study. The study was carried out in accordance with the Declaration of Helsinki and Guidelines for Good Clinical Practice. Informed consent was obtained from all study participants. The study included a total of 90 volunteers, aged

between 18 and 65 years old, with 45 personnel working in a setting with potential for radiation exposure (Exposed Group) and 45 personnel in a setting without radiation exposure (Control Group).

Persons with decompensated heart failure, valvular disease or recent atherosclerotic heart disease (last three months), a history of revascularization, recent infection, malignancy, liver/kidney failure, autoimmune/inflammatory disease, the use of corticosteroids or nonsteroidal anti-inflammatory drugs, blood dyscrasia and hematologic diseases were excluded from the study.

The study population included the personnel exposed to radiation in the anesthesia application areas outside of the operation room (interventional cardiology, interventional radiology, interventional gastroenterology), and the personnel exposed to radiation in the operation room. Participant's age, sex, duration and distance of radiation exposure were recorded.

All participants with radiation exposure were submitted to dosimetry. Personal dose equivalent for all body Hp 10 and personal dose equivalent for skin Hp 0.07 were determined with the Optically Stimulated Luminescence (OSL) dosimetry technique. Dosimetry values in the month of the study period (Hp 10, Hp 0.07) and the values of the year of the study (total Hp 10, total Hp 0.07) were recorded.

Plasma sampling, analytical procedure and laboratory methods

Venous blood samples were collected through the antecubital vein from the volunteer exposed and control groups. Plasma blood samples were centrifuged at 3500 rpm for 10 minutes at 4°C, within 30 minutes after the sample collection from the participants. Serum obtained was kept frozen at -80°C. Serum TDH measurements were made with the spectrophotometric method described by Erel and Neselioglu. First, reducible disulfide bounds were reduced in order to form functional thiol groups. After reaction with DTNB [5,50-dithiobis-(2-nitrobenzoic acid)], reducer sodium borohydride in the medium was depleted and removed using formaldehyde, and thus all thiol groups including reduced and native thiol groups were determined. Half of the difference between total thiol and native thiol was calculated as the disulfide level. After measuring native thiols (SH) and total thiols (SH + SS) and the amount of disulfides (SS), disulfide/total thiol ratio (Index 1), disulfide/native thiol ratio (Index 2) and native thiol/total thiol ratio (Index 3) were calculated.⁸

Albumin cobalt binding test was used to determine the presence of IMA. This test was carried out by an addition of 50 mL 0.1% cobalt (II) chloride ($\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$) (Sigma-Aldrich Chemie GmbH Riedstrasse 2, Steinheim, Germany) to the patient's serum. After centrifugation, incubation was made for 10 minutes to allow the binding of albumin cobalt, and 50 mL 1.5 mg.mL⁻¹ Dithiothreitol (DDT) was added. After centrifugation, following incubation for 2 minutes, 1.0 mL 0.9% sodium chloride solution was added to decrease binding capacity. Absorbance of the samples were read at 470 nm using a spectrophotometer, and the results were expressed in Absorbance Units (AU).¹² IMA/Serum Albumin Ratio (IMAR) was also calculated.

Statistical analysis

Results of this study were analyzed with the SPSS 19.0 software. Continuous values were expressed as mean \pm Standard Deviation and categorical values were expressed as number and percentage, n (%). Normal distribution of the data was analyzed with Kolmogorov-Smirnov test, histogram and \pm SD. Non-parametric data of the groups were compared with the Mann-Whitney *U* test and parametric data with the Independent *t* test. Categorical data were analyzed with the Chi-Square test. ROC curve analysis was performed in all exposed volunteers in order to determine usability of the parameters (albumin, IMAR, native thiol, total thiol) to distinguish participants who were exposed from the control, and the sensitivity and specificity were calculated for the optimal cut-off values. Correlations between TDH parameters, albumin and IMA was evaluated with the Pearson correlation analysis; $p < 0.05$ values were considered statistically significant.

Results

Demographic and clinical features of participants

A total of 45 exposed and 45 control subjects were included in the study. The mean age was 36.11 ± 6.30 years in the Exposed Group, and 34.73 ± 6.59 years in the Control Group ($p = 0.314$). F/M ratio was 8 (17.8%)/37 (82.2%) in the Exposed Group and 12 (26.7%)/33 (73.3%) in the Control Group ($p = 0.447$).

Subgroup analysis was performed between the personnel exposed to radiation in the anesthesia application areas out of the operation room – Operation room (-)/(n=19) and the personnel exposed to radiation in the operation room – Operation room (+)/(n=26). The mean age was 37.10 ± 7.10 years in the Operation room (-) Group, and 35.38 ± 5.67 years in the Operation room (+) Group ($p=0.372$). F/M ratio was 5 (26.3%)/14 (73.7) in the Operation room (-) and 3 (11.5%)/23 (88.5%) in the Operation room (+) groups ($p=0.299$). Duration of radiation exposure was 5.30 ± 2.40 years in the Operation room (-), and 6.61 ± 5.14 years in the Operation room (+) groups ($p=0.314$).

Laboratory primary outcomes of patients

Albumine levels were $4.47 \pm 0.53 \text{ g.dL}^{-1}$ and $5.32 \pm 0.49 \text{ g.dL}^{-1}$ in the Exposed Group and the Control Group, respectively ($p < 0.001$). IMA levels were found as $0.76 \pm 0.12 \text{ AU}$ and $0.74 \pm 0.08 \text{ AU}$ in the exposed and the control groups, respectively ($p = 0.457$). Native Thiol levels were $487.60 \pm 62.91 \mu\text{mol.L}^{-1}$ and $541.41 \pm 69.48 \mu\text{mol.L}^{-1}$ in the Exposed Group and the Control Group, respectively ($p < 0.001$). Total thiol levels were $556.64 \pm 61.60 \mu\text{mol.L}^{-1}$ and $607.64 \pm 71.36 \mu\text{mol.L}^{-1}$ in the Exposed Group and the Control Group, respectively ($p < 0.001$). Disulfide levels were found as $34.51 \pm 7.82 \mu\text{mol.L}^{-1}$ and $33.11 \pm 5.17 \mu\text{mol.L}^{-1}$ in the Exposed Group and the Control Group, respectively ($p = 0.319$) (Table 1).

Table 1 Demographic, clinical features and laboratory primary outcomes of patients.

	Group exposed (n = 45)	Group control (n = 45)	95% CI lower/upper	p-value
Age (years)	36.11 ± 6.30	34.73 ± 6.59	-1.32/4.07	0.314
Gender				0.447
F	8 (17.8%)	12 (26.7%)		
M	37 (82.2%)	33 (73.3%)		
Weight (kg)	73.25 ± 16.20	71.37 ± 12.68	-4.89/6.67	0.592
Albumin (g.dL ⁻¹)	4.47 ± 0.53	5.32 ± 0.49	-1.36/-0.62	< 0.001
IMA (AU)	0.76 ± 0.12	0.74 ± 0.08	-0.02/0.06	0.457
IMAR (IMA/Albumin) (%)	0.17 ± 0.04	0.14 ± 0.02	0.01/0.04	< 0.001
Native thiol ($\mu\text{mol.L}^{-1}$)	487.60 ± 62.91	541.41 ± 69.48	-81.57/-26.03	< 0.001
Total thiol ($\mu\text{mol.L}^{-1}$)	556.64 ± 61.60	607.64 ± 71.36	-78.92/-23.06	< 0.001
Disulfide ($\mu\text{mol.L}^{-1}$)	34.51 ± 7.82	33.11 ± 5.17	-1.37/4.18	0.319
Disulfide/Total thiol (%)	7.24 ± 2.26	6.21 ± 1.35	0.24/1.80	0.011
Disulfide/Native thiol (%)	6.26 ± 1.61	5.50 ± 1.04	0.19/1.33	0.009
Native thiol/Total thiol (%)	87.46 ± 3.23	88.98 ± 2.08	-2.66/-0.37	0.010

IMA, Ischemia Modified Albumin; AU, Absorbance Units; IMAR, Ischemia Modified Albumin/Albumin.

Table 2 Comparison of laboratory secondary outcomes of patients.

	Operation room (-) (n = 19)	Operation room (+) (n = 26)	95% CI lower/upper	p-value
Age (years)	37.10 ± 7.10	35.38 ± 5.67	-2.12/5.56	0.372
Gender				0.299
F	5 (26.3%)	3 (11.5%)		
M	14 (73.7%)	23 (88.5%)		
Duration of radiation exposure	5.30 ± 2.40	6.61 ± 5.14	-3.87/1.27	0.314
Albumin (g.dL ⁻¹)	4.41 ± 0.56	4.52 ± 0.52	-0.44/0.21	0.502
IMA (AU)	0.72 ± 0.10	0.79 ± 0.13	-0.14/0.002	0.086
IMAR (IMA/Albumin) (%)	0.16 ± 0.03	0.18 ± 0.04	-0.03/0.01	0.418
Native thiol ($\mu\text{mol.L}^{-1}$)	463 ± 56.96	505.0 ± 62.33	-77.81/-4.59	0.028
Total thiol ($\mu\text{mol.L}^{-1}$)	531.73 ± 54.13	574.85 ± 61.26	-78.65/-7.57	0.019
Disulfide ($\mu\text{mol.L}^{-1}$)	33.95 ± 10.16	34.92 ± 5.73	-5.77/3.84	0.687
Disulfide/Total thiol (%)	7.51 ± 2.91	7.04 ± 1.68	-0.91/1.85	0.499
Disulfide/Native thiol (%)	6.43 ± 2.04	6.14 ± 1.24	-0.69/1.28	0.551
Native thiol/Total thiol (%)	87.12 ± 4.09	87.71 ± 2.49	-2.57/1.39	0.551
Hp 10 (mSv)	0.25 ± 0.06	0.21 ± 0.04	0.002/0.06	0.035
Hp 0.07 (mSv)	0.29 ± 0.07	0.22 ± 0.04	0.02/0.09	< 0.001
Hp 10 total (mSv)	0.63 ± 0.52	0.21 ± 0.04	0.21/0.62	< 0.001
Hp 0.07 total (mSv)	0.70 ± 0.57	0.22 ± 0.04	0.24/0.70	< 0.001

IMA, Ischemia Modified Albumin; AU, Absorbance Units; IMAR, Ischemia Modified Albumin/Albumin; Hp 10, Personal dose equivalent for all body; Hp 0.07, Personal dose equivalent for skin; mSv, millisievert.

Secondary laboratory outcomes of patients

Albumine levels were $4.41 \pm 0.56 \text{ g.dL}^{-1}$ and $4.52 \pm 0.52 \text{ g.dL}^{-1}$ in the Operation room (-) and the Operation room (+) groups, respectively ($p = 0.502$). Native Thiol levels were $463 \pm 56.96 \mu\text{mol.L}^{-1}$ and $505.0 \pm 62.33 \mu\text{mol.L}^{-1}$ in the Operation room (-) and the Operation room (+) groups, respectively ($p = 0.028$). Total thiol levels were $531.73 \pm 54.13 \mu\text{mol.L}^{-1}$ and $574.85 \pm 61.26 \mu\text{mol.L}^{-1}$ in the Operation room (-) and the Operation room (+) groups, respectively ($p = 0.019$). Hp 10 (mSv) levels were 0.25 ± 0.06 and 0.21 ± 0.04 in the Operation room (-) and the Operation room (+) groups, respectively ($p = 0.035$). Hp 0.07 (mSv) levels were

0.29 ± 0.07 and 0.22 ± 0.04 in the Operation room (-) and the Operation room (+) groups, respectively ($p < 0.001$). Hp 10 total (mSv) levels were 0.63 ± 0.52 and 0.21 ± 0.04 in the Operation room (-) and the Operation room (+) groups, respectively ($p < 0.001$). Hp 0.07 total (mSv) levels were 0.70 ± 0.57 and 0.22 ± 0.04 in the Operation room (-) and the Operation room (+) groups, respectively ($p < 0.001$) (Table 2).

ROC and correlation analysis

ROC analysis were performed for albumin, IMAR, native thiol and total thiol to distinguish the Exposed Group from the

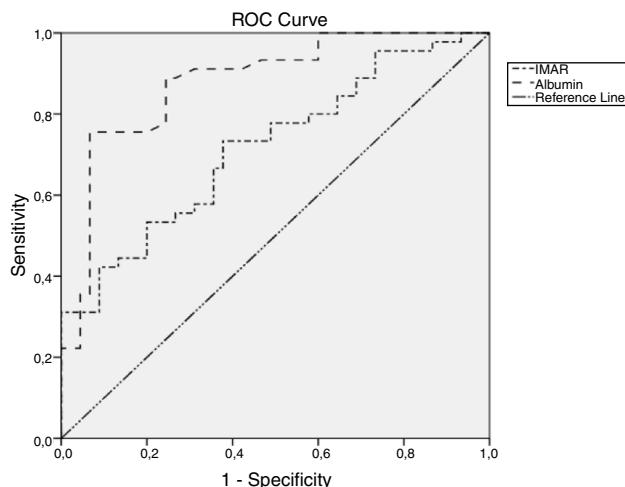


Figure 1 ROC curves for serum IMAR, albumin concentrations to differentiate Exposed Group from the Control Group.

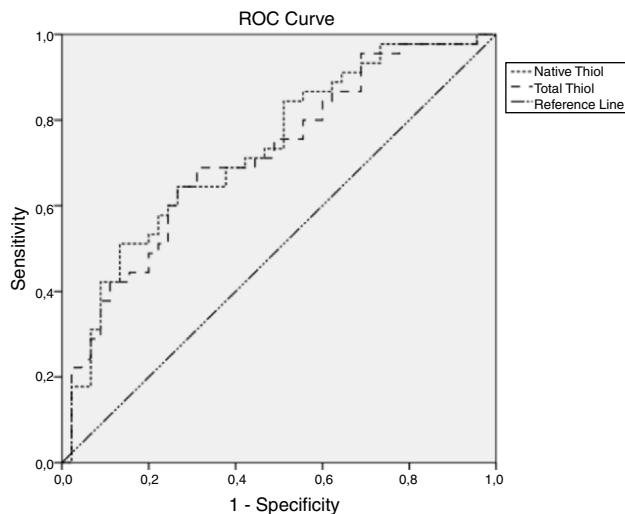


Figure 2 ROC curves for serum native thiol, total thiol concentrations to differentiate Exposed Group from the Control Group.

Control Group. ROC curves are given in Figs. 1 and 2, and the results of the ROC analysis were summarized in Table 3.

There is a negative correlation between albumine and IMA, IMAR, Index I and Index II ($p=-0.339$, $p=0.001/p=-0.787$, $p<0.001/p=-0.302$, $p=0.004/p=-0.311$, $p=0.003$; respectively). There is a positive correlation between albumin and native thiol, total thiol and Index III ($p=0.543$, $p<0.001/p=0.538$, $p<0.001/p=0.309$, $p=0.003$; respectively). There is a

negative correlation between IMAR and native thiol and total thiol ($p=-0.462$, $p<0.001/p=-0.460$, $p<0.001$; respectively).

Discussion

LDIR exposure may cause an increase in the activity of Reactive Oxygen Species (ROS) and accelerate cellular aging by impairment of biopolymers. With radiation exposure, inflammatory mediator release and continuous production of ROS and nitric oxide increases the toxic effects of radiation induced inflammation on normal tissues.¹³ ROS activity is controlled by various enzymatic and non-enzymatic antioxidants. Insufficiency in the ability of balancing increased ROS formation with antioxidants results in oxidative stress, a complex stressor for cells that manifests as increased oxidative molecular damage to biomolecules, e.g. oxidation of lipids, oxidative modification of nitrogenous bases etc.¹⁴

The relationship between LDIR and production of reactive species has been widely described.¹⁵ At the same time the correlation between genetic damage and oxidative damage clearly explains the role of ionizing radiation in the formation of ROS.¹⁶

Generally, this low rate of exposure comes from natural sources in the air, soil, rocks and cosmic rays (accounting for 2–2.5 mSv/year), while the rest is acquired from man-made sources such as medical procedures (periodic X-Ray, CT scans and others) and industrial activities.¹⁷ Oxidative stress in persons exposed to radiation in the workplace have recently been reported, however the number of these studies is limited.^{18–20}

In the light of these facts, persons exposed to radiation were composed from the anesthesia application areas outside of the operation room (interventional cardiology, interventional radiology, interventional gastroenterology), and the personnel exposed to radiation in the operation room.

Thiols are a class of organic compounds containing a functional carbon-bonded Sulphydryl group (SH) that can be oxidized by disulfide (–S–S–) bond formation. Thiols are critical in the prevention of oxidative stress. In case of loss of thiol groups, mechanisms that change the structure and function of proteins begin to emerge. Oxidizers cause thiols to undergo oxidation reaction and form disulfide bonds. In the event of oxidative stress, cysteine residues are oxidized and reversible mixed disulfides are formed between the low molecular mass thiols and the protein thiol groups. Disulfide bonds can be reduced back to thiol groups. In this way, TDH is maintained. Thiol levels may also be reduced without an increase in disulfide. This may be due to excessive consumption or insufficient uptake of thiols due to use in

Table 3 ROC analysis.

	AUC	p	95% CI	Sensitivity	1 – Specificity	Cut-off
Albumin	0.879	< 0.001	0.807–0.951	75.6	93.3	4.80
IMAR (IMA/Albumin)	0.717	< 0.001	0.612–0.822	73.3	62.2	0.14
Nativethiol	0.731	< 0.001	0.627–0.834	68.9	62.2	510
Total thiol	0.717	< 0.001	0.611–0.822	68.9	68.9	573

IMA, Ischemia Modified Albumin; IMAR, Ischemia Modified Albumin/Albumin; AUC, Area Under Curve; CI, Confidence Interval.

other syntheses instead of disulfide transformations.^{8,21} Furthermore, the absence of a significant increase in disulfide levels can be explained by the fact that only thiol groups may be greatly affected in this process. Like our findings, there are many studies showing a decrease in thiol levels but no increase in disulfide levels.^{20,22} The low level of thiol reflects a decrease in antioxidant activity. In our study, we concluded that antioxidant levels were decreased in patients exposed to low dose ionizing radiation due to a low thiol level without a change in disulfide level.

IMA is a form of serum albumin in which the N-terminal amino acids are unable to bind to transition metals. In ischemia, the generation of free radicals and acidosis results in changes in the ability of the N-terminus of albumin to bind to transition metal ions and to initiate IMA generation. Ischemia and oxidative stress are the major determinants of forming IMA.²³ There isn't much information about the formation or the clearance of IMA in the plasma. However, IMA is known to increase and decrease back down to normal levels within 24 h after angioplasty, suggesting that it has a shorter half-life when compared to albumin.²⁴ The increase in serum IMA is thought to be either due to over-production or due to decreased clearance.²⁵

In normal conditions, the IMA level is negatively correlated with the albumin level. The duration and severity of oxidative stress related tissue hypoperfusion, and accompanying disorders affect the serum level and kinetics of IMA. Assuming that the type of mechanisms such as tissue hypoxia, hypoperfusion, inflammation and oxidative damage that cause an increase in serum IMA levels is determined by serum IMA kinetics,²³ IMA production mechanism is complex in radiation exposure and it is still unclear.

The cause of low albumin is that oxidative stress causes molecular modifications in human serum albumin, such as carbonylation and the formation of advanced oxidation protein products and advanced glycation end products. However, it has been demonstrated that a common biochemical assay (the bromocresol green assay) may result in "apparent" hypoalbuminemia, and that this assay underestimates albumin concentrations when the protein is oxidatively modified.²⁶

In our study, albumin level was significantly lower in the group exposed to radiation. Although no significant difference was found between IMA levels, IMAR level was significantly higher in the exposed group. Taken together, the results of the above mentioned studies and the present study show that the antioxidant process is very dynamic, complex, and multifactorial.

Optimal environmental conditions are essential in order to provide awareness of the workers on this issue, to use newly developed techniques and tools, and to provide individual and social safety. The use of bio-dosimeters and physical dosimeters is important to support physical measurements of radiation exposure with biological indices, because routine physical dosimeters may not be properly used, they may be insufficient because of wrong placement, and may largely vary due to individual sensitivity levels.²⁷

In our study, in the subgroup analysis, physical dosimeters of the personnel exposed to radiation were evaluated. Physical dosimetry values were significantly higher in the Operation room (-) Group compared to the Operation room (+) Group. The difference in this dosimetry was reflected

only on the native thiol and total thiol values from the oxidative stress markers. Native thiol and total thiol levels were significantly lower in the Operation room (-) Group compared to the Operation room (+) Group. In parallel to the dosimetry values, antioxidant levels dropped more significantly in the Operation room (-) Group. In the light of these results, awareness should be established in healthcare personnel exposed to radiation with the programs for protection against radiation and raising awareness.

Limitations

One of the limitations of both this study and the previous studies is that an exact measurement of the time, amount and distance of the exposure, which may affect the exposure could not be done. As another limitation, this study was conducted with a small group.

There are workplace factors such as surgical smoke produced by the use of volatile anesthetic agents, contagious agents, electrocautery or laser systems, and cleaning agents and solvents that may potentially disrupt redox homeostasis. Therefore, these unmeasured factors may also play a role. Despite the presence of closed anesthesia systems and properly running modern cleaning devices, volatile anesthetic gas exposure is inevitable for operation room personnel.²⁸ Therefore, we constituted our Operation room (+) personnel from those exposed to radiation and were working in operation rooms where closed anesthesia systems were used and induction with mask ventilation was not performed.

Conclusion

According to the results of this study, the sensitivity and specificity of IMAR, native thiol and total thiol are high in making a distinction between the personnel exposed to LDIR in the anesthesia application areas and those without radiation exposure. Our results support that TDH may be applied in order to evaluate oxidative stress after LDIR exposure and can be developed as a novel method. Impaired TDH in personnel exposed to radiation both in the Operation room (-) and Operation room (+) groups, the decreased levels of native thiol and total thiol that act as antioxidants, and increased IMAR levels indicate that antioxidant supplementation can be administered in personnel exposed to LDIR chronically. Awareness of being in danger of oxidative stress should be established in personnel exposed to LDIR in the anesthesia application areas, both necessary measures should be taken and antioxidant therapy should be administered.

Conflicts of interest

The authors declare no conflicts of interest.

References

- Ozasa K. Epidemiological research on radiation-induced cancer in atomic bomb survivors. *J Radiat Res.* 2016;57:112–7.

2. Tubiana M, Feinendegen LE, Yang C, et al. The linear no-threshold relationship is inconsistent with radiation biologic and experimental data. *Radiology*. 2009;251:13–22.
3. Seong KM, Kwon T, Seo S, et al. Perception of low dose radiation risks among radiation researchers in Korea. *PLoS One*. 2017;12:e0171777.
4. United Nations Scientific Committee on the Effects of Atomic Radiation [UNSCEAR]. Biological effects at low radiation doses. United Nations Scientific Committee on the Effects of Atomic Radiation. UNSCEAR Report Vol. II: Effects (Annex G). United Nations: New York; 2000. http://www.unscear.org/docs/publications/2000/UNSCEAR_2000_Report_Vol._II [accessed 16.01.18].
5. National Research Council [NRC]. Health risks from exposure to low levels of ionizing radiation: BEIR VII Phase 2. Washington, DC: The National Academies Press; 2006. <http://dx.doi.org/10.17226/11340>.
6. International Commission on Radiological Protection. The 2007 recommendations of the International Commission on Radiological Protection. ICRP Publication 103. Annals of the ICRP 37; 2007. <https://journals.sagepub.com/doi/pdf/10.1177/ANIB.37.2-4> [accessed 08.01.18].
7. Banne AF, Amiri A, Pero RW. Reduced level of serum thiols in patients with a diagnosis of active disease. *J Anti Aging Med*. 2003;6:327–34.
8. Erel O, Neselioglu S. A novel and automated assay for thiol/disulphide homeostasis. *Clin Biochem*. 2014;47:326–32.
9. Taverna M, Marie AL, Mira JP, et al. Specific antioxidant properties of human serum albumin. *Ann Intens Care*. 2013;3:2–7.
10. Sokolowska M, Krezel A, Dyba M, et al. Short peptides are not reliable models of thermodynamic and kinetic properties of the N-terminal metal binding site in serum albumin. *Eur J Biochem*. 2002;269:1323–31.
11. Roy D, Quiles J, Gaze DC, et al. Role of reactive oxygen species on the formation of the novel diagnostic marker ischaemia modified albumin. *Heart*. 2006;92:113–4.
12. Bar-Or D, Lau E, Winkler JV. A novel assay for cobalt albumin binding and its potential as a marker for myocardial ischemia a preliminary report. *J Emerg Med*. 2000;19:311–5.
13. Multhoff G, Radons J. Radiation, inflammation, and immune responses in cancer. *Front Oncol*. 2012;2:58.
14. Halliwell B, Gutteridge J. Free radicals in biology and medicine. Oxford, UK: Oxford University Press; 2007.
15. Smith JT, Willey NJ, Hancock JT. Low dose ionizing radiation produces too few reactive oxygen species to directly affect antioxidant concentrations in cells. *Biol Lett*. 2012;8:594–7.
16. Galván I, Bonisoli Alquati A, Jenkinson S, et al. Chronic exposure to low-dose radiation at chernobyl favours adaptation to oxidative stress in birds. *Funct Ecol*. 2014;28:1387–403.
17. Pandey B, Kumar A, Tiwari P, et al. Radiobiological basis in management of accidental radiation exposure. *Int J Radiat Biol*. 2010;86:613–35.
18. Malekiran AA, Ranjbar A, Rahzani K, et al. Oxidative stress in radiology staff. *Environ Toxicol Pharmacol*. 2005;20:215–8.
19. Eken A, Aydin A, Erdem O, et al. Induced antioxidant activity in hospital staff occupationally exposed to ionizing radiation. *Int J Radiat Biol*. 2012;88:648–53.
20. Koc U, Tan S, Ertem AG, et al. Evaluation of thiol-disulphide homeostasis in radiation workers. *Int J Radiat Biol*. 2017;93:705–10.
21. Kundu H, Ates I, Kiziltunc E, et al. A novel oxidative stress marker in acute myocardial infarction; thiol/disulphide homeostasis. *Am J Emerg Med*. 2015;33:1567–71.
22. Emre S, Demirseren DD, Alisik M, et al. Dynamic thiol/disulfide homeostasis and effects of smoking on homeostasis parameters in patients with psoriasis. *Cutan Ocul Toxicol*. 2017;36:393–6.
23. Sahin A, Turkoglu S, Tunc N, et al. Is ischemia-modified albumin a reliable tool for the assessment of acute pancreatitis? *Ther Clin Risk Manag*. 2018;14:627–35.
24. Sinha MK, Vazquez JM, Calvino R, et al. Effects of balloon occlusion during percutaneous coronary intervention on circulating ischemia modified albumin and transmyocardial lactate extraction. *Heart*. 2006;92:1852–3.
25. Gafsou B, Lefevre G, Hennache B, et al. Maternal serum ischemia-modified albumin: a biomarker to distinguish between normal pregnancy and preeclampsia? *Hypertens Pregn*. 2010;29:101–11.
26. Michelis R, Kristal B, Snitkovsky T, et al. Oxidative modifications impair albumin quantification. *BBRC*. 2010;401:137–42.
27. Ramos M, Montoro A, Almonacid M, et al. Radiation effects analysis in a group of interventional radiologists using biological and physical dosimetry methods. *Eur J Radiol*. 2010;75:259–64.
28. Kozanhan B, Inanlı I, Deniz CD, et al. Dynamic thiol disulphide homeostasis in operating theater personnel exposed to anesthetic gases. *Am J Ind Med*. 2017;60:1003–9.