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ARTICLE

# Investigation of the effects of gamma radiation on plasma levels of Zn, Cu, Mn and Se in nuclear medicine staff

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**Abstract –** We assessed possible changes in the levels of some trace elements among nuclear medicine staff. This study was carried out on 30 nuclear medicine staff and 10 individuals as a control group. After the blood samples were collected, serum levels of trace elements were measured using atomic absorption spectroscopy (AAS). Mean Zn levels in the control group (89.75 ± 17.35 μmol/l) were significantly ($p = 0.002$) higher than in the exposed group (70.91 ± 14.46 μmol/l). Increased duration of exposure was significantly associated with reduced zinc levels ($p = 0.005$). Furthermore, the 5-year average dose received was adversely and significantly correlated with zinc concentrations ($p = 0.019$). No significant difference was observed in the Cu level between control group (93.85 ± 25.33 μmol/l) and staff worker group (85.6 ± 21.66 μmol/l) ($p = 0.32$). A positive significant correlation was observed between exposure time and reduced Cu levels ($p = 0.05$). No difference was found in mean Mn and Se levels between both groups according to exposure time. Declined Zn and Cu levels may be considered as one of the possible mechanisms of oxidative damages induced by gammas rays. Therefore, an antioxidant treatment could be recommended for people who work in medical radiation centers.

**Keywords:** gamma radiation / zinc / manganese / copper / manganese / nuclear medical staff

## 1 Introduction

Ionizing radiation has been used in various diagnostic methods such as radiography, nuclear medicine and CT-scan (Szewczak *et al.*, 2013). Although ionizing radiation is important in diagnosis and treatment of different diseases, they can exert some pathological effects on human body (Huda and Gordon, 1989; Kumar *et al.*, 2012) which is depended on radiation type, exposure time and dose (Dolezal, 2008).

Gamma radiation is a common type of radiation that can split water and lead to the formation of reactive oxygen species (ROS) (Lousada *et al.*, 2016; Zheng *et al.*, 2017), which in turn cause oxidative stress and cell death. Since ROS such as hydroxyl radicals ($OH^{\bullet}$) and superoxide anion ($O_2^{\bullet}$) have unpaired electron in their structure, they can interact with DNA, proteins and lipids, leading to oxidative damages and cells death (Zheng *et al.*, 2016; Chuenpee *et al.*, 2017). Nevertheless, human cells contain several enzymatic and non-enzymatic antioxidants that play critical roles in free radicals scavenging (Wojcik *et al.*, 2012). Some of enzymatic antioxidants (metalloenzymes) contain essential elements such as zinc (Zn), copper (Cu), manganese (Mn) and selenium (Se) in their structure that play critical roles in the cellular redox (oxidation-reduction) system. Therefore, a decreased level of these elements may be associated with reduced activity of several enzymatic antioxidants and, subsequently with a massive production of ROS and oxidative stress.

Several lines of studies considered the effects of different types of radiation on levels of some trace elements. For example, Shahbazi-Gahrouei and Adbolahi (2014) investigated association between high background radiation exposures with trace plasma levels of Cu, Zn, Fe and Mg of hot springs workers (Shahbazi-Gahrouei and Adbolahi, 2014). They showed that Cu concentration in employees was lower than that of control group, but zinc and iron had significant increase in employee group. Magnesium average concentration in employee was lower than that of control group; however, this difference was not statistically significant (Shahbazi-Gahrouei and Adbolahi, 2014).

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Zinc is a critical element in human body that not only serves as an antioxidant, but also is essential for the normal functioning of various proteins, especially metalloenzymes, transcription factors and zinc finger proteins (Perera *et al.*, 2016; Ajina *et al.*, 2017). Previous studies showed that Zn is necessary for many physiological processes such as growth, neural system functioning, reproduction and immunity (Colagar *et al.*, 2009; Skalny *et al.*, 2015). Selenium is another significant element that serves as cofactor and free radicals scavenger in glutathione peroxidase (GPX) structure (Michalska-Mosiej *et al.*, 2016). Copper and manganese are shown to be involved in suppressing of ROS-induced DNA damages (Dell'Acqua *et al.*, 2017; Versieren *et al.*, 2017). Copper also plays as a cofactor for redox enzymes, mitochondrial respiration, iron absorption, and free radical inhibition (Perera *et al.*, 2016; Alarifi *et al.*, 2017). Manganese not only participates in the structure of several enzymes such as mitochondrial superoxide dismutase (SOD), glutamine synthetase and arginase, but also is involved in the activation of several hydrolases, transferases, and carboxylases (Gonzalez-Garcia *et al.*, 2016).

Decreased level of some trace elements, especially elements involved in redox system, may be one mechanism of gamma radiation effect on human body. Depletion of these trace elements can be associated with a deficiency in antioxidant defense system, and consequently oxidative stress. A few studies investigated the effect of gamma radiation on plasma levels of some trace elements; however, the critical role of Zn, Cu, Se, and Mn against ROS and oxidative damages is illustrated. Since nuclear medicine workers are frequently exposed to radiation, especially gamma rays, we aim to study the effects of gamma radiation on plasma levels of Zn, Cu, Mn, and Se.

## 2 Materials and methods

### 2.1 Subjects

In this cross sectional study, a total number of 30 nuclear medicine staff and 10 healthy individuals were entered into the study between 2016 and 2017. This study was approved by the institutional review board and ethical committee of, Baqiyatallah University of Medical Sciences (ir.bmsu.rec.1395.390). Written informed consents were signed by all individuals. A questionnaire containing demographic data of all individuals was also filled before examinations. Healthy individuals were selected from out of hospital and no abnormalities were found in terms of physical examination or their laboratory results. They also did not have history of exposure to gamma radiation. The control subjects were matched to the nuclear medicine staff based on age, weight and gender.

Inclusion criteria for nuclear medicine staff were:

- documentary exposure to gamma radiation for at least 5 years;
- identified dose of exposure;
- staff who worked in a nuclear medicine department where they were directly exposed to gamma rays and;
- voluntary participation in the study. Those who have experienced the use of anti-inflammatory, trace elements or antioxidant drugs at the time of the examination were excluded from the study.

### 2.2 Measurement of Zn, Se, Cu, and Mn in serum

A total of 20 ml blood samples were collected from the antecubital veins of participants and healthy donors after an overnight fast during the first examination. Serum samples were separated by centrifugation (EBA21, Hettich, Germany) at 4000 rpm for 7 min and then stored at −20 °C until trace element measurement. The studied trace elements were measured by flame atomic absorption spectroscopy (AAS) method with graphite furnace (GBC-GF500, Australia). HCl 0.1N was applied for protein precipitation before the assessment of Cu and Zn levels, while Triton X-100 and Trichloroacetic acid were used for the assessment of Mn and Se levels, respectively. After that, supernatants were injected into the apparatus.

### 2.3 Statistical analysis

Demographic and clinical characteristics of all individuals were reported as means ± SD. An independent student *t*-test was considered to compare the mean of some parameters between the nuclear medicine staff and control groups. Descriptive statistics was applied for the analysis of frequencies among participants. A Chi-Square program was used to compare the frequency of some data between different groups. The Pearson correlation test and linear regression were used to analyze and examine the relationship between element concentrations and other parametric data. Data were analyzed using SPSS software (SPSS Version 19.0; IBM SPSS Inc., Chicago, IL, USA) and a $p \leq 0.05$ was considered as significant.

## 3 Results

The results from demographic characteristics in the control and nuclear medicine staff groups can be seen in Table 1. In total, 30 nuclear medicine staff (17 males and 13 females) and 10 healthy individuals (6 males and 4 females) were entered into the study. The mean age of individuals in the control and nuclear medicine staff groups was 37.0 ± 5.77 and 41.83 ± 10.38 years, respectively. Any significant difference has been shown ($p = 0.171$). The mean exposure time in the nuclear medicine staff group was 6.76 ± 2.04 years. The 5 year average dose received was 21.63 ± 48.61 mSv. Information on other demographic data, especially history of several diseases, is presented in Table 1. There was no significant difference in mean percentage of disease history between the two groups.

Table 2 shows the mean concentration of trace elements in the blood of both groups. The control group had a significant ($p = 0.002$) higher zinc value (89.75 ± 17.35 µmol/l) compared to the nuclear medicine staff group (70.91 ± 14.46 µmol/l). There was no significant difference in mean of other elements between the two groups.

A negative significant correlation was found between the dose of 5 year-exposure and Zn levels (Fig. 1; $p = 0.019$). We also found a negative significant relationship between work experience of workers at hospitals and Cu levels (Fig. 2; $p = 0.05$) levels in blood. Interestingly, we also found a

**Table 1.** Demographic characteristics of control and nuclear medicine staff groups.

| Parameters | Control | Workers | *p*-value |
|---|---|---|---|
| Age | 37.0 ± 5.77<br>(29–47 years) | 41.83 ± 10.38<br>(28–68 years) | 0.171 |
| Gender | | | |
| Male | 6 (60%) | 17 (56.66%) | 0.85 |
| Female | 4 (40%) | 13 (43.33%) | |
| Weight | 79.9 ± 6.43<br>(70–94 kg) | 75.36 ± 12.83<br>(55–100 kg) | 0.293 |
| Exposure time (years) | – | 6.76 ± 2.04<br>(1–12) | – |
| Dose of exposure during 5 years (mSv) | – | 21.63 ± 48.61<br>(0.1–254.02) | – |
| Smoking | | | |
| Yes | 3 (30%) | 2 (6.63%) | 0.058 |
| No | 7 (70%) | 28 (93.33%) | |
| Alcohol using | | | |
| Yes | 2 (20%) | 0 | 0.012 |
| No | 8 (80%) | 30 (100%) | |
| Opium | | | |
| Yes | 0 | 2 (6.33%) | 0.4 |
| No | 10 (80%) | 28 (93.33%) | |
| Exercise | | | |
| Yes | 4 (40%) | 18 (60%) | 0.27 |
| No | 6 (60%) | 12 (40%) | |
| Milk use | | | |
| Yes | 9 (90%) | 13 (43.33%) | 0.01 |
| No | 1 (10%) | 17 (56.66%) | |
| Cardiac disease | | | |
| Yes | 0 | 2 (6.66%) | 0.4 |
| No | 10 (100%) | 28 (93.33%) | |
| Thyroid dysfunction | | | |
| Yes | 0 | 5 (16.66%) | 0.16 |
| No | 10 (100%) | 25 (83.33%) | |
| Hypertension | | | |
| Yes | 0 | 5 (16.66%) | 0.16 |
| No | 10 (100%) | 25 (83.33%) | |
| Cancer | | | |
| Yes | 0 | 0 | – |
| No | 10 (100%) | 30 (100%) | |
| Digestive disease | | | |
| Yes | 0 | 3 (10%) | 0.29 |
| No | 10 (100%) | 27 (90%) | |
| Hyperlipidemia | | | |
| Yes | 2 (20%) | 4 (13.33%) | 0.6 |
| No | 8 (80%) | 26 (86.66%) | |
| Anemia | | | |
| Yes | 0 | 2 (6.66%) | 0.4 |
| No | 10 (100%) | 28 (93.33%) | |
| Diabetes | | | |
| Yes | 0 | 3 (10%) | 0.29 |
| No | 10 (100%) | 27 (90%) | |
| Supplement | | | |
| Yes | 4 (40%) | 10 (35.71%) | 0.8 |
| No | 6 (60%) | 18 (64.28%) | |
| Skin nail disease | | | |
| Yes | 1 (10%) | 0 | 0.079 |
| No | 9 (90%) | 30 (1005) | |

**Table 2.** Comparison of trace elements between the control and nuclear medicine staff groups.

| Parameters | Control | Workers | *p*-value |
|---|---|---|---|
| Selenium (μmol/l) | 1.71 ± 0.35 | 2.13 ± 1.12 | 0.34 |
| Zinc (μmol/l) | 89.75 ± 17.35 | 70.91 ± 14.46 | 0.002 |
| Copper (μmol/l) | 93.85 ± 25.33 | 85.6 ± 21.66 | 0.32 |
| Manganese (μmol/l) | 1.15 ± 0.45 | 1.17 ± 0.46 | 0.9 |

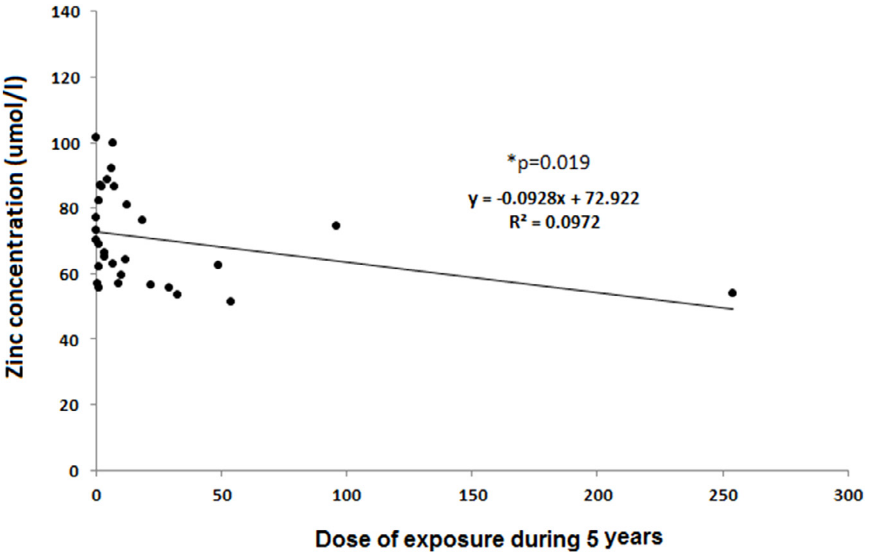

**Fig. 1.** Correlation between dose of 5 years-exposure and zinc levels. A significant negative correlation was observed between dose of exposure and zinc levels ($p = 0.019$).

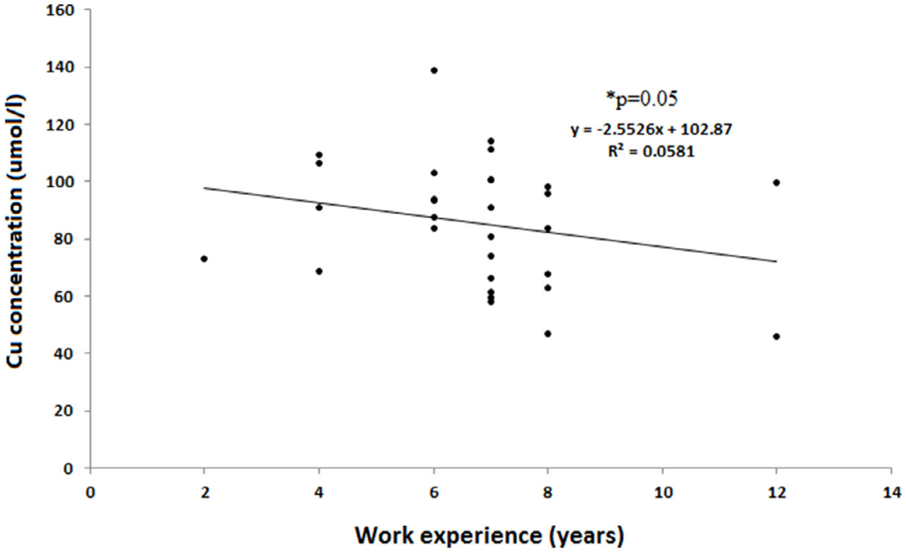

**Fig. 2.** Correlation between work experience of workers and Cu levels. A significant negative correlation was observed between dose of exposure and Cu levels ($p = 0.05$).

significant positive correlation between Zinc and Copper levels (Fig. 3; $p = 0.0000$). Decreased levels of zinc were associated with decreased values of copper in radiated individuals.

## 4 Discussion

In this study, the effects of gammas on plasma levels of Zn, Cu, Mn, and Se were considered for the first time among

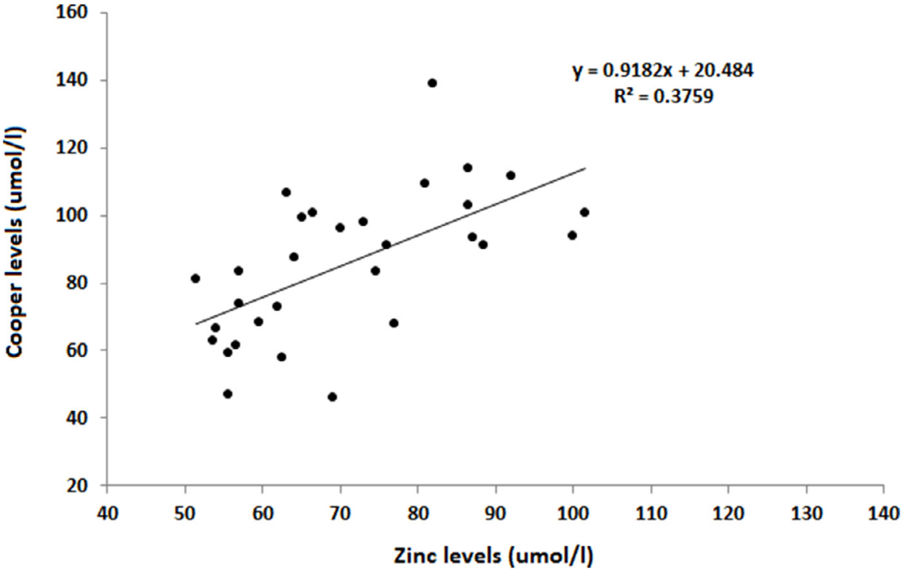

**Fig. 3.** Correlation between zinc and copper in radiated workers. A significant positive correlation was observed between Zinc and Copper levels ($p = 0.0000$).

nuclear medicine staff exposed for 5 years at least. Our data have revealed that these individuals exposed to gamma radiation had significantly lower mean value of Zn levels compared to non-exposed persons. Increased exposure dose was significantly associated with reduced contents of zinc in blood. Additionally, this effect was dose-dependent. We found that, there is a significant negative correlation between Zn levels and the gamma dose received by nuclear medicine staff for 5 years. Although we could not find a significant difference in mean of Mn and Se contents between the two groups, a mild trend was observed toward lower mean concentration of Cu in serum of the nuclear medicine staff compared to the control group. Increased exposure time to gamma radiation was also significantly associated with declined mean value of Cu in blood.

Very limited studies that investigated the effects of gamma radiation on levels of some trace elements are available. For example, in a study by Ono *et al.* (1998) the effects of gamma radiation were evaluated on serum melatonin contents, lipid peroxidation and Zn values in the brain tissue of exposed rats (Ono *et al.*, 1998). The authors found that increased exposure time to gamma radiation was associated with significant reduction in mean of Zn levels and enhanced level of melatonin in the brain of exposed rats; however, non-significant change was observed in lipid peroxidation. Given the antioxidative role of melatonin, these authors suggested that increased content of melatonin might suppress lipid peroxidation.

Ebrahiminia *et al.* (2008) considered relationship between occupational exposure and concentration of Cu, Zn, Fe, and Mg in radiology and radiotherapy workers (Ebrahiminia *et al.*, 2008). There was no significant difference in mean of Zn, Fe, and Mg levels between technician and control groups; however, Cu values obtained in technician group were higher than those of control group. The mean contents of Zn, Cu and Fe in blood and hair of X-ray technicians and non-X-ray technicians were also previously assessed (Chatterjee *et al.*, 1994). The results revealed a significant increase in Zn, Cu, and Fe concentrations in X-ray technicians' hair. But in blood, Zn and Cu were depleted, whereas Fe was increased (Chatterjee *et al.*, 1994). Although this study considered the effects of X-ray instead of gamma radiation on blood trace elements, these data are in accordance with the results obtained in our study. In a previous study, Protasova *et al.* (2001) investigated the level of some trace elements including Al, Cd, Co, Cu, Fe, Mg, Mn, Mo, P, Pb, S, and Zn in blood serum and hairs several years after exposure to low doses of ionizing radiation (Protasova *et al.*, 2001). The results showed altered concentration in mean of these trace elements between exposed and non-exposed individuals.

According to these studies and our findings, decreased level of Zn and Cu levels in plasma of technicians exposed to gammas may partially explain pathological effects of ionizing radiation on health. Zn and Cu are significant cofactors useful to several antioxidant enzymes such as Zn/Cu-SOD enzyme that scavenges intercellular ROS. Interestingly, we observed a significant positive correlation between Zn and Cu elements, in which increased levels of zinc was associated with increased levels of copper. Recent evidences have revealed that massive production of ROS, oxidative stress and DNA damages are the major mechanisms by, which gamma radiation mediates pathological effects. In an experimental study, Sudprasert *et al.* (2006) demonstrated that higher exposure time to gamma radiation at different doses (5 and 10 cGy) is associated with DNA damages, oxidative damages to nucleotides and deficiency of DNA repair system in whole blood and peripheral lymphocytes (Sudprasert *et al.*, 2006). The authors suggested that genotoxic effects of gamma radiation may be mediated through oxidative DNA damages and reduced repair capacity. In another study, Mishra (2004) found that gamma radiation causes enhanced production of intercellular ROS, oxidative stress and, subsequently apoptosis in *in vitro* model (Mishra, 2004). Vucic *et al.* (2006) demonstrated that gamma radiation causes inhibition of DNA synthesis, cell division and as the result cytotoxicity (Vucic *et al.*, 2006). Additionally, the authors observed overexpression of Mn-SOD and Cu/Zn-SOD enzymes by 3.5 fold after exposure to gamma radiation, which suggests the critical roles of these enzymes in reducing the gamma radiation-induced oxidative stress. Given the critical function of Zn and Cu in free radical scavenging, reduced contents of these trace elements possibly trigger radiation-oxidative damages.

In conclusion, our findings have revealed that not only plasma levels of Zn and Cu declined after exposure to gamma radiation in nuclear medicine staff, but also this effect is dose-depended. Given the critical roles of Zn and Cu as cofactors for several antioxidant enzymes, reduced levels of these trace elements in blood should be considered in the context of antioxidant defenses. Further studies are necessary to consider the relationship between radiation exposures, these trace elements level in the blood and the activity of antioxidant metalloenzymes such as Mn-SOD and Zn-SOD. However, we should mention that the changes in Zn and Cu concentration could be due to differences in the food habits of the participants, not detected by the questionnaire. Furthermore, decrease in Zn and Cu concentrations in the blood could be a consequence of SOD activation, not as a starting point. In such a case, the observed decrease does not induce a higher level of damage. Given these limitations to the present study, the measurements of SOD activities, together with Cu and Zn measurements, should be done in future studies, to assess a possible correlation and to clarify this point.

## Conflict of interests

The authors declare that they have no conflicts of interest in relation to this article.

## Ethical statement

This study was approved by the institutional review board and ethical committee of Baqiyatallah University of Medical Sciences (ir.bmsu.rec.1395.390). This study was supported from a personal funding. Written informed consents were signed by all individuals.

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