

Original Article

The Comparison of Lead and Zinc Plasma Levels in Breast Cancer Patients with Standard Values

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ABSTRACT

Purpose- Breast cancer is the second leading cause of death among women. One in eight women will be diagnosed with breast cancer in their life period. There are several risk factors for the progress of carcinogen cells. Zinc and lead have crucial roles in oxidative stress and any changes in their level can enhance the progress of carcinogen cells. The purpose of this study is to discover the level of zinc and lead in the plasma of breast cancer patients.

Methods- One hundred breast carcinoma diagnoses was confirmed by pathological samples and the results were compared with standard values. The amount of these elements was observed in the blood by an atomic absorption.

Result- Zinc plasma level in patients was found to be 50.59 ± 4.72 ($\mu\text{g/dl}$) with the p value of $p=0.003$ which is lower than the standard value ($80 \mu\text{g/dl}$). On the other hand, the plasma lead level was identified to be 6.24 ± 1.173 ($\mu\text{g/dl}$) in patients and zero in the standard value.

Conclusion- According to the observation, breast cancer patients had a higher lead level than the standard value and a lower zinc level. Zinc acts as an important free-radical scavenger to protect cells and a deficiency of that can increase the progress of carcinogen cells. Therefore, the use of trace elements and also the chelators of heavy metals are necessary to prevent breast cancer in high risk individuals.

1. Introduction

Breast cancer is a major health concern for women around the world including Iran. It was reported more than 502,000 women lost their lives. Breast cancer is the second most common cancer after lung cancer. It is also the most common cause death by cancer among women. Moreover, the incidence of the diagnosed patient among Iranian women is increasing drastically [1]. Nonetheless, the incidence of breast cancer in Asian women is lower compared to women in western countries [2].

Trace elements are involved in the development of breast cancer. However, the relationship between them is not exactly clear [3]. The genetic material

in DNA is transcribed into RNA molecules that are eventually translated into proteins with a specific function. Transcription factors are used to control the production of specific RNA molecules through their sequences-specific association with the DNA. For example, one class of transcription factors is known as the zinc-finger. Zinc finger is a DNA binding protein that consists of a series of amino acids arranged in 'hairpin' structure in which each domain is stabilized through coordination to zinc. The zinc ions do not interact with the DNA, but they are necessary for the stability of the protein and to maintain the hairpin fold, which enables the amino acids interaction with specific parts of the DNA. Protein loops could also be held together,

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for example by disulfide bridges, but these can be easily cleaved via reduction in contrast to bonds between zinc and Cys or His. In addition, there are not redox side reactions that could cause DNA damage. Therefore, zinc has an important role in our biological system [4].

Lead is a significant toxicant which can induce an inauspicious effect in humans' health. People are susceptible to high doses of lead. Exposure to lead can cause different health problems, including neurological, reproductive, renal and hematological. Lead can promote mutagenesis when is coupled with alkylating and oxidizing DNA- damaging agent. Epidemiologic studies have demonstrated a possible association between the occupational exposure to lead and specifically lung, kidney and stomach cancers [5].

This study was designed to investigate the plasma level of zinc and lead in breast carcinoma patients.

2. Materials and Methods

2.1. Setting and Patients

This study was organized in Imam Hospital of Sari located in the north of Iran. One hundred patients with breast carcinoma diagnosis were confirmed by pathological samples and the results were compared with standard values.

2.2. Sampling and Analysis

A 5 ml blood sample was taken from each patient and healthy volunteers; then the samples were moved to special tubes and were heated in lukewarm water (37°C) for 1 hour. The samples were centrifuged (1500 rpm) and frozen at -20°C after the serum isolation.

To determine the zinc and lead concentrations in serum samples, standard zinc and lead solutions

were prepared. Four standard zinc solutions (0.1, 1, 5, 10 ppm) and four standard lead solutions (0.5, 1, 10, 50 ppm) were made. After the samples were defrosted, 0.5 ml of serum sample for the zinc assessment and another 0.5 ml for the lead assessment were isolated. The sera of samples were moved to 5 ml volumetric flasks, and then glycerol solution 5% and 10% were used for the determination of zinc and lead concentration. Zinc and lead serum levels were assayed by flame Atomic Absorption Spectrophotometer (AAS)(CT Chrometech 1500) with λ_{\max} =217.8 nm for lead level and λ_{\max} =213.9 nm for zinc level determination. Then, the concentrations were determined following the preparation of calibration curves.

2.3. Statistical Analysis

To be able to compare the lead and zinc level of patients with standard values, students' T-test has been conducted. P-value <0.05 is considered as a significant difference. In addition, SPSS version 14 software was used for data analysis.

3. Results

100 patients were screened for this study and the date was compared with the standard rate. The ages of patients were between 50 -70 years old and all the patients were female. Levels of lead and zinc are shown in Table 1. According to Table 1, the zinc plasma level in patients was found to be 50.59 ± 4.72 ($\mu\text{g}/\text{dl}$) with the p-value of ≤ 0.003 . A comparison of the zinc level in patient individuals with the standard rate demonstrate that the level of zinc is significantly lower than the standard value (80 $\mu\text{g}/\text{dl}$). On the other hand, the plasma lead level was identified to be 6.24 ± 1.173 ($\mu\text{g}/\text{dl}$) in patients and zero in standard value. According to this data, the plasma lead level is higher than the standard value, considering p-value ≤ 0.003 .

Table1. Level of zinc and lead in cancer breast patients and standard values.

Metal	Patient	Standard	P-value
Lead	6.24 ± 1.173 ($\mu\text{g}/\text{dl}$)	0 ($\mu\text{g}/\text{dl}$)	0.003
Zinc	50.59 ± 4.72 ($\mu\text{g}/\text{dl}$)	80 ($\mu\text{g}/\text{dl}$)	0.003

4. Discussion

The study identified that the zinc content in the breast cancer patients was lower than the standard content of zinc. Zinc is one of the important trace elements in human body for many biological functions [6]. It is a necessary component of more than 300 enzymes needed to maintain fertility in adults and healthy immune system, repair wounds, synthesizing of proteins, reproduce cells and more importantly protect against free radicals. Zinc acts as an important free-radical scavenger to protect cells [7]. Zinc regulates the DNA, RNA synthesis and it influences the hormonal regulation of cell growth. Zinc participates in diverse cellular processes as a cofactor for many enzymes and it is also involved in the gene expression through the transcription factor [8]. Therefore, zinc deficiency can impact directly or indirectly on the process of cancer development. Other risk factors such as the lack of physical activity, poor diet, saturated fat rich diet and lacking fruits and vegetables, obesity, drinking alcohol and combined hormone replacement therapy increases risk factors for breast cancer [9]. Moreover, nutritional deficiency of zinc and environmental exposure to lead and N-Nitrosamines plays a crucial role in increasing the risk of breast cancer [10]. Dietary deficiencies in zinc can lead to the single and double-strand DNA breaks and oxidative modifications to DNA that increase the risk for cancer development [11].

Zn, SOD(Superoxide Dismutase) and Cu help the body to defend against Reactive Oxygen Species (ROS) [12]. This function is used to remove the superoxide anion (O_2^-). A low dietary zinc intake and high concentration of phytate which is a powerful chelator of divalent metals lead to zinc deficiency [13]. The pathological signs of zinc deficiency include stunted growth, impaired parturition (dystocia), neuropathy, decreased food intake, diarrhea, dermatitis, hair loss, bleeding tendency, hypotension and hypothermia [14]. Severe zinc deficiency is rare, whereas mild deficiency is highly common even in developed countries [15].

Foods such as red meat, seafood, as well as several plant sources, like whole grains and legumes are excellent sources of zinc [16]. However, the zinc in these sources are much less bioavailable. Therefore, vegetarians may also be at risk of zinc deficiency [17].

Lead is one of the toxic elements among the heavy metals. According to the literature, there is an association between the exposure to inorganic lead and cancers such as lung and stomach [18]. In our studies, it was found that lead levels of breast cancer patients was significantly higher than standard value [19]. Lead in vitro inhibits the rapier activity of API which is the major endonuclease for repairing mutagenic and cytotoxic a basic sites in DNA [20].

In addition to the factors that were identified in this study, there are other factors such as family history, exposure to carcinogens and diets which could contribute to the development of cancer.

5. Conclusion

In conclusion, breast cancer patients had a higher lead level than the standard value and a lower zinc level. This study demonstrates the critical role of trace elements such as zinc and heavy metal like lead as a risk factor for the development of breast cancer. According to our results and other studies, a favorable use of trace elements and also the chelators of heavy metals are necessary to prevent breast cancer in high risk individuals.

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References

- 1- M.Enayatrad, N.Amoori, H.Salehiniya, Epidemiology and Trends in Breast Cancer Mortality in Iran. *Iranian Journal of Public Health*, 44(3), 430-431. 2015.
- 2- H.A.Otaghvar, M.Hosseini, A.Tizmaghz, G.Shabestanipour, A review on metastatic breast cancer in Iran. *Asian Pacific Journal of Tropical Biomedicine*, 5(6), 429-433. 2015.
- 3- J. F.Feng, L.Lu, P.Zeng, Y.H.Yang, J.Luo, Y.W.Yang, D.Wang, Serum total oxidant/antioxidant status and trace element levels in breast cancer patients. *International journal of clinical oncology*, 17(6), 575-583. 2012.
- 4- J.J.R.Frausto da silva, R.J.P.William, The biological chemistry of the elements., 2nd ed. New York. 1991.
- 5- D.R.Juberg, Lead and human health, 2nd ed, New York. 1997.

- 6- SR.Powell, The antioxidant properties of zinc. *J Nutr*; 130: 1447S – 54S. 2000.
- 7- T.M. Bray, W.J. Bettger, The physiological role of zinc as an anti- oxidant. *Free RadicBiol Med*; 8:281–91. 1990.
- 8- R.J.Cousins, A role of zinc in the regulation of gene expression. *ProcNutrSoc*; 57:307–11. 1998.
- 9- HH.Sandstead, AS.Prasad, AR.Schulert, Z.Farid, A.MialeJr, S.Bassilly, et al, Human zinc deficiency, endocrine manifestations and response to treatment. *Am J ClinNutr*; 20:422 – 42. 1967.
- 10- KM.Hambidge, NF. Krebs, L.Miller Evaluation of zinc metabolism with use of stable-isotope techniques: implications for the assessment of zinc status. *Am J ClinNutr*; 68:410S – 3S. 1998.
- 11- A.Federico, P.Iodice, P.Federico, A.Del Rio, MC.Mellone, G.Catalano, Effects of selenium and zinc supplementation on nutritional status in patients with cancer of digestive tract. *Eur J ClinNutr*; 55:293 – 7. 2001.
- 12- D.Conte, S.Narindrasorasak, B.Sarkar, In vivo and in vitro iron-replaced zinc finger generates free radicals and causes DNA damage. *J BiolChem*; 271:5125–30. 1996.
- 13- RE.Kelly, MI.Mally, DR.Evans, The dihydroorotase domain of the multifunctional protein CAD. Subunit structure, zinc content, and kinetics. *J BiolChem*; 261:6073–83. 1986
- 14- PJ.Fraker, P.Jardieu, J.Cook Zinc deficiency and immune function. *Arch Dermatol*; 123:1699 – 701. 1987.
- 15- AS.Prasad, Zinc deficiency. *BMJ*; 326:409–10. 2003.
- 16- AS.Prasad Zinc deficiency in humans: a neglected problem. *JAmColl Nutr*;17:542.1998.
- 17- P.Wakimoto, G.Block, Dietary intake, dietary patterns, and changes with age an epidemiological perspective. *J Gerontol A BiolSci Med Sci*;56:65–80. 2001.
- 18- T.V.Lam, P.A govino , X.Niu et al, linkage study of cancer risk among lead-exposed workers in New jersey , *sci, Total Environ* , 372:455-462.2007.
- 19- D.R.McNeill,H.K. Wong, A.Narayana , D.M. Wilson, lead promotes abasic site accumulation and comutagenesis in mammalian cell by inhibition the major abasic endonuclease Ape 1. *Molecular Carcinogen*,42:91-99.2006.
- 20- S.E.Schober, L.B. Mirel and B.I. Graubard et al, Blood lead Levels and death from all causes, cardiovascular disease and cancer: Results from the NHANES III mortality study. *Environ. Health perspectives*, 114: 1538-1541.2006.