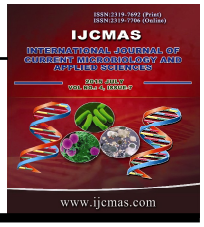
Int.J.Curr.Microbiol.App.Sci (2015) 4(8): 812-816

International Journal of Current Microbiology and Applied Sciences
ISSN: 2319-7706 **Volume 4 Number 8 (2015) pp. 812-816**
http://www.ijcmas.com



Original Research Article

Determination the Levels of Zinc and Copper in Patients with Leukemia

Hussein K. Alkufi*

Department of Clinical and Laboratory Sciences, College of Pharmacy, Thi-Qar University, Iraq
**Corresponding author*

Keywords

Antioxidant, Copper, Leukemia, Zinc

A B S T R A C T

Leukemia is the most common type of blood cancer in which both of zinc and copper levels are altered resulting in many metabolic and physiological disorders. This alteration is controversial, the reason why this study is worked. This study comprised 50 patients with leukemia (chronic and acute) where 35 males and 15 females, their mean ages were (48.50 ± 15.06, 34.30 ± 12.05 years for males and females respectively while the control group included 15 healthy participants. During the period from December 2012 to March 2013, the cases with leukemia were enrolled from patients admitted to Al –Sader teaching Hospital. The design composed of two groups, the study group which included fifty patients whom afflicted with leukemia, there were Control group which included healthy individuals consisted from 15 persons. Zinc and copper were determined according to the colorimetric determination using the available kits. Zinc levels were significantly lower ($p < 0.001$) in acute leukocyte leukemia (ALL) and chronic myelogenous leukemia (CML) than in the control. While copper levels were demonstrated a significant ($p < 0.001$) increased in chronic myelogenous leukemia (CML) and acute lymphocyte leukemia (ALL) compared with control group.

Introduction

Leukemia is the most common type of blood cancer including white blood cells (leukocytes) which are potent infection fighters. Excessive increasing in immature leukocytes number resulted from the malicious tumors of the arising and infiltrating of the hematopoiesis tissues of the bone marrow. It is considered as a progressive disorder which occurred in chronic and acute forms. Moreover, another classification of leukemia depends on the damaged cells such as myeloid and lymphoid cells (Hope *et al.,* 2004).

Many factors are involved in leukemia, such as abnormality of the chromosomes, viruses, irradiations, and chemicals (Bloomfield *et al.,* 1986)

Cancer patients usually have inadequate energy and protein intakes, increased metabolic rate and abnormalities in energy, carbohydrate, lipid and protein metabolism. Cancer therapy with chemotherapy and radiation therapy is also potentially damaging to nutritional status (Wesdorp *et al.,* 1983). Trace elements are basic

foodstuffs as well as they consider a frequent contaminated dietary of the environment (Gottlieb and Drewinko, 1975). It is performing the processing of the physiologic and metabolic body function (Mertz, 1981). Zinc, the more prolific intracellular trace elements, exhibits the preventive effect on the gene mutations and transformation the cells through its effective anti-oxidant factor by its ability to obligation and protection the sulphydryls of the protein from radical attack. Furthermore, it organizes the catalytic activity of many enzymes which belong to the main categories of the mammary enzymes. In addition to its stabilizing effect in the tertiary and quaternary of protein structures and its association to certain sites in protein (Ho, 2004; Washabaugh and Collins, 1986).

Zinc role as antioxidant include remove superoxide ion through the enzyme of superoxide dismutase by the obstruction formation of hydroxyl ion through the activation of oxidation of transition metals such as, copper and iron (Conte *et al.,* 1996). Reactions of detoxification and responses to the stress depend on the metallothioneins activity and expression regulation (Bloomfield *et al.,* 1986; Malemud, 2006). Deficit or excessive levels zinc as a trace elements has effect on the balance of the global cellular anti-oxidant, and several carcinogen effects, which includes, DNA repairing, synthesis of DNA, implication on mutations proliferation of cells, apoptosis and differentiation, these had important role in the maintaining DNA integrity (Fong and Magee, 1999; Nasulewicz *et al.,* 2004), and second it involved in membrane transport, nerve conduction and muscle contraction and also in the function of sub-cellular systems such as mitochondria (Senturker *et al.,* 1997). In addition, trace elements such as zinc and copper act as antioxidants (Bakan *et al.,* 2003) for leukemia the distribution levels of these trace elements represents the uncontrolled proliferation of cell as seen in leukemia. This study was undertaken to examine the levels of essential elements, zinc and copper in patients with leukemia.

Materials and Methods

This study of trace elements in leukemia is carried out by assisting a pathologist who has had a wide experience in this field, samples are collected from patients according to the approval ethics in biochemical research. The period range was from December 2012 to March 2013. Patients with leukemia were recruited from those attending Al –Sader teaching hospital.

A group of studied population comprised fifty patients (chronic and acute) whom afflicted with leukemia (35 males and 15 females), their mean ages were 48.50 ± 15.06 and 34.30 ± 12.05 years for males and females respectively. While control group involved healthy individuals and it included 15 persons which are selected according to sex, age, to match study group patients. The control group was used only for comparing serum zinc and copper levels. Blood samples collected from both groups and saved in plain tubes for subsequent analysis. Both of zinc and copper are determined according to the colorimetric determination using the available kits (Pasquinelli, 1984; Abe *et al.,* 1989).

The descriptive data of patients with leukemia and controls in studied population are summarized in table 1.

Statistical analysis

Results are expressed as mean and standard deviation (mean ± SD). Student-t test was used to determine the difference between groups. P value <0.05 was considered statistically significant.

Results and Discussion

During the current research the following results were obtained. Zinc levels were significantly lower ($p < 0.001$) in acute leukocyte leukemia (ALL) and chronic myelogenous leukemia (CML) than in the control. While copper levels were significantly increased in the leukemic group, chronic myelogenous leukemia (CML) and acute lymphocyte leukemia (ALL), compared to the control group ($p < 0.001$) as demonstrated in table 2 and figure 1.

Leukemia is a neoplastic disease that is susceptible to essential elements alterations such as zinc and copper. Studies related to zinc and copper levels in leukemia development are controversial and deserve further analysis. Therefore, in this study we analyzed and followed potential role of zinc and copper as antioxidant for oxidative damage in leukemia patients by analyzing serum levels of previous antioxidant.

In this prospective study of leukemia patients zinc levels are decreased when compared with controls. The significant decreased of zinc levels in patient groups could be expected to offer a lot of factors are involved in leukemia and the oxidative stress related it.

Thus, the role of development leukemia stage with decreased zinc is clear and the explanations in many prospective studies demonstrated that leukemic cells contain much less zinc than normal lymphocytes, suggesting an error in zinc metabolism. Studies by Beguin *et al.* (1987) and Mrozek *et al.* (2006) investigated the association between zinc deficiency and DNA replication and RNA polymerization. Whereas zinc deficiency associated with T cell function, impaired cellular immune function and occurrence of a lymphoid system (Zowczak *et al.,* 2001; Choudhury *et al.,* 2003). Increasing evidence of clinical and experimental indicates that leukemia plays a major role in the damage antioxidant balance by results in disturbances of thymic hormone activity and T-cell maturation (Gürses *et al.,* 2000).

On the other hand, the lifestyle of the patients in the studied population could be impact on the levels of trace elements since almost of them live in districts area and have a bad situation of living. However, administration of leukemic patients with zinc treatment has beneficial effect (Caporaso *et al.,* 2004).

In the present study copper levels were found to be increased in patients groups compared with controls. In particular, copper was transition metal, and an essential element in the biological systems, and its function is related to this redox properties (Tracey and Carter, 2005; Harrison *et al.,* 2000).

These finding were consisted with that elevation of serum copper have been found in the pathologic conditions which accompanied by increased rate of tissues destruction and / or proliferation (Bakan *et al.,* 2003)

In another study of antioxidant activity in leukemia, Beguin *et al.* (1987) suggested that elevated leukemia burden as marker of development leukemia stage that is independent of other risk like increased levels of serum copper. Our results point to a possible relationship between high levels of copper and developed stage of leukemia. Also, it has suggested that accumulated of copper may enhance tumorigenesis (Nasulewicz *et al.,* 2004).

Table.1 Descriptive data of leukemic patients and controls in studied population

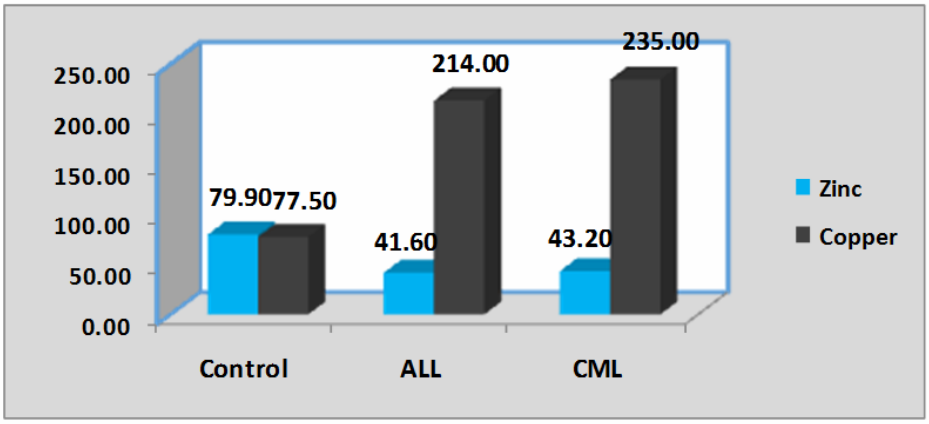
Age (mean± SD)			No. of cases	percent	occupation	places
Sex	**Males**	48.50±15.06	35	70%	Earner(30) Student(5)	District(28) Al-Najaf(2)
	Females		15	30%	House wife(15)	District(12) Al-Najaf(3)
Controls			15	30%	Employee(13) Student(2)	Al-Najaf(15)

Table.2 Association between zinc and copper levels in leukemia patients

Variables		No.	Zinc (µg/dl)	Copper (µg/dl)
Control		15	74.90± 2.84	77.50 ± 4.81
patients	ALL	30	41.60 ± 14.90*	214.00 ± 70.20*
	CML	20	43.2± 13.60*	235.00± 69.90*

*P< 0.001 compared to the Control groups.

Figure.1 Comparison between zinc and copper levels in control, ALL, and CML groups



The present study indicated imbalances in the levels of zinc and copper of leukemia patients may adversely affect the biological processes of DNA that lead to the uncontrolled proliferation of cells and defect DNA function. The disturbances are consisted respective with the stage of the disease.

References

Abe, A. *et al.* 1989. Determination of copper in serum and plasma. *Clin. Chem.*, 35(4): 552–554.

Bakan, N., Taysi, S., Yilmaz, Ö. *et al.* 2003. Glutathione peroxidase, glutathione redutase, Cu-Zn superoxide dismutase activities, glutathione, nitric oxide, and

malodialdehyde concentrations in serum of patients with chronic lymphocytic leukemia. *Clin. Chim. Acta.*, 338(1–2): 143–149.

Beguin, Y., Brasseur, F., Weber, G. *et al.* 1987. Observation of serum trance elements in chronic lymphocytic leukemia. *Cancer,* 60(15): 1842–1846.

Bloomfield, C.D., Goldman, A.I., Alimena, G. *et al.* 1986. Chromosomal abnormalities identify high-risk and low-risk patients with acute lymphoblastic leukemia. *Blood,* 67(2): 415–20.

Caporaso, N., Marti, G.E., Goldin, L. 2004. Perspectives on familial chronic lymphocytic leukemia: genes and the environment. *Seminars Hematol.*, 41: 201–206.

Choudhury, S., Zhang, R., Frenkel, K., *et al.* 2003. Evidence of alterations in base excision repair of oxidative DNA damage during spontaneous hepatocarcinogenesis in Long Evans Cinnamon rats. *Cancer Res.*, 63: 7704–7707.

Conte, D., Narindrasorasak, S., Sarkar, B. 1996. *In vivo* and *in vitro* iron-replaced zinc finger generates free radicals and causes DNA damage. *J. Biol. Chem.*, 271(9): 5125–5130.

Fong, L.Y., Magee, P.N. 1999. Dietary zinc deficiency enhances esophageal cell proliferation and N- nitrosomethyl benzylamine (NMBA)-induced esophageal tumor incidence in C57BL/6 mouse. *Cancer Lett.*, 143(1): 63–69.

Gottlieb, J.A., Drewinko, B. 1975. Review of the current clinical status of platinum coordination complexes in cancer chemotherapy. *Cancer*, 59: 621–8.

Gürses, A., Ulya, M., Feride, D., Dilek, B. *et al.* 2000. High prevalence of chronic magnesium deficiency in T cell lymphoblastic leukemia and chronic zinc deficiency in children with acute lymphoblastic leukemia and malignant lymphoma. *Leuk. Lymph.*, 39(5–6): 555–562.

Harrison, M.D., Jones, C.E., Solioz, M., Dameron, C.T. 2000. Intracellular copper routing: the role of copper chaperones. *Trends Biochem. Sci.*, 25(1): 29–32.

Ho, E. 2004. Zinc deficiency, DNA damage and cancer risk. *J. Nutl. Biochem.*, 15: 572–578.

Hope, K.J., Jin, L., Dick, J.E. 2004. Acute myeloid leukemia originates from a hierarchy of leukemic stem cell classes that differ in self-renewal capacity. *Nat. Immunol.*, 5: 738–43.

Malemud, C.J. 2006. Matrix metalloproteinases (MMPs) in health and disease: an overview. *Front Biosci.*, 11: 1696–1701.

Mertz, W. 1981. The essential trace elements. *Science*, 213: 580–583.

Mrozek, K., *et al.* 2006. Reviews the genetic pathways that are altered in the pathogenesis of acute myeloid leukemia. *Hematology*, 111: 169–177.

Nasulewicz, A., Mazur, A., Opolski, A.J. 2004. Review role of copper in tumor angiogenesis--clinical implications. *Trace Elem. Med. Biol.*, 18(1): 1–8.

Pasquinelli, F. 1984. Diagnostic technique in laboratory, colorimetric determination of zinc in serum, plasma, and urine. *Chimica Clinica Acta*, 197: 209–220.

Prasad, A.S. 2003. Zinc deficiency. *Br. Med. J.*, 326: 409–410.

Senturker, S., Karahalil, B., Inal, M. *et al.* 1997. Oxidative DNA base damage and antioxidant enzyme levels in childhood acute lymphoblastic leukemia. *FEBS Lett.*, 416(3): 286–290.

Tracey, M.C., Carter, J.M. 2005. Ethnicity variables in the incidence rates of leukemia in New Zealand populations: implications for stem-cell transplantation. *Am. J. Hematol.*, 79: 114–118.

Washabaugh, M.W., Collins, K.D. 1986. Dihydro-orotase from *Escherichia coli*. Sulfhydryl group metal ion interactions. *J. Biol. Chem.*, 261: 5920–5929.

Wesdorp, R.I.C., Krause, R., Meyenfeldt, M.F. 1983. Cancer cachexia and its nutritional implications. *Br. J. Surg.*, 70: 352–5.

Zowczak, M., Iskra, M., Torliski, L. *et al.* 2001. Analysis of serum copper and zinc concentrations in cancer patient. *Biol. Trace Elem. Res.*, 82: 1–8.