

Estimation of copper & zinc in plasma of acute lymphoplastic leukemia

Rashid M. Yousuf*, Entedar R. Sarhat**, Shaker M. Al-Jobori***, Mossa M. Marbut****,

* Dept. of Physics, College of Science, Mosul University,

** College of Dentistry, Tikrit University

***Iraqi Atomic Energy Committee

**** Dept. of Physiology, College of Medicine, Tikrit University.

Abstract

Several works have shown that a definite relationship that exists between trace elements & certain diseases. the aim of this study is to investigate the change in plasma copper & zinc of acute lymphoplastic leukemia. 41 subjects were participating in this study; 20 healthy subjects & 21 patients suffer from acute lymphoblastic leukemia (ALL). Blood samples were collected & plasma copper & zinc concentrations were measured. Plasma zinc is significantly lower in ALL patients than control by 11% ($p < 0.01$), whereas plasma copper is higher in ALL patients than control by 14.7%. In the present study, p.cu/p.zn ratio of control (19%) was lower than that of ALL patients (24.7%). The higher ratio of patients is due to reciprocal changes of copper & zinc. This index may better than copper or zinc alone.

Key words: acute lymphoplastic leukemia, plasma copper, zinc

Introduction

The availability of effective treatment for malignant diseases depends on the presence of sensitive biological markers that correlates with disease activity. Several works have shown that a definite relationship that exists between trace elements & certain diseases (1, 2,3). Plasma copper (p.cu), plasma zinc (p.zn) and selenium are among several biochemical that have been used (4,5,6). Many reports had suggested that copper & zinc might reflect disease activity (4, 5).

Therefore, the aim of this study is to investigate the change in plasma copper & zinc of acute lymphoplastic leukemia.

Patients & Methods

41 subjects were participating in this study; 20 healthy subjects & 21 patients suffer from acute lymphoblastic leukemia (ALL). The study was conducted at children hospital in Baghdad medical city. Blood samples were collected & plasma copper & zinc concentrations were measured by X-ray fluorescence technique (XRF) (6). The XRF involves the measurement of intensity of an admitted X-ray from the sample. Plasma copper / plasma zinc ratio (p.cu/pzn ratio) was determined by dividing p.cu

concentration by p.zn concentration & multiply by 100. Data were analyzed by using student T test & presented as mean & standard deviation (SD).

Results

20 patients suffering from ALL (aged 6.8 ± 4 years) & 21 healthy subjects aged 7.9 ± 3.5 years were participated in this study.

Table 1 shows the age of patients, the mean, standard deviation, & the range of plasma zinc & copper. Plasma zinc is significantly lower in ALL patients than control by 11% ($p < 0.01$). Whereas plasma copper is higher in ALL patients than control by 14.7% ($p < 0.01$).

It was found that the range of p.cu in patients was 1.103 to 1.879 ug/ml (mean value is 1.568 ± 0.184), while, the range for control subjects was 0.931 to 1.774 mg/ml (mean 1.367 ± 0.199).

Moreover, the range of p.zn in patients was 5.584 to 7.293 (mean 6.39 ± 0.478 ug/ml), while the range of p.zn in control was 6.568 to 8.088 (mean 7.195 ± 0.475 ug/ml). There is 11.2% reduction in

plasma zinc in ALL patients comparing with control subjects.

There was a significant difference in P.cu / p.zn ratio between ALL patients (24.7%) & control subjects (19%). In other words, P.cu / p.zn ratio is higher in patients than control subjects.

Discussion

Plasma copper was found to have a positive relationship with disease activity that p.cu concentration increases as disease activity increases. This finding was reported previously in other type of cancer such malignant lymphoma (3) & breast cancer (4). But this result was not reported previously in ALL.

In the present study, the plasma zinc of ALL patients is lower than that of control subjects ($p < 0.01$). Zinc is active element everywhere in the body as co-factor for more than 70 enzymes; also it helps in the function of white blood cell (WBC) in immune system. The zinc content of WBC in human leukemic patients is decreased to about 10% of normal amount (7,8). Also, this finding was reported previously in other type of cancer such malignant lymphoma (3,9) & breast cancer (4), but not reported previously in ALL. For this reason & others, zinc supplementations have been reported to improve & increase immune function (10, 11). This effect may be especially important in the elderly according to double blind study that found a zinc supplement is important for patients with recurrent infection (12,13,14).

By using plasma copper / p.zn ratio, which is show better index for pathological changes of disease activity. In the present study, p.cu/p.zn ratio of control (19%) was lower than that of ALL patients (24.7%). The higher ratio of patients is due to reciprocal changes of copper & zinc. This index may better than copper or zinc alone.

Therefore, conclusion could be drawn as plasma copper, plasma zinc & its ratio may be useful indexes for diseases activity & a good biological marker for ALL patients. So, that zinc supplement have been reported to increase immune function (15,16).

There are claims that copper aids the body in functions such as the healing process, expelling toxins from the body, and preventing heart problems. There are also claims that copper actually promotes cancer growth. Proponents of this theory recommend a low copper diet and use of chelating agents that bind to copper and promote its elimination from the body (see Chelation Therapy), (17,18,19,20).

Copper is a trace mineral that is needed for many important body processes. Animal studies have shown that copper is useful in maintaining antioxidant defenses. Antioxidant compounds block the action of activated oxygen molecules, known as free radicals, which can damage cells. While the involvement of copper in the cancer process via antioxidant effects is still unclear, copper complexes have been shown to have anti-cancer properties in lab studies (21,22,23,24).

Other lab and animal studies suggest that high copper levels may be linked to liver cancer and brain tumors. More recently, many studies have shown that blood copper levels are higher in several types of cancer as well as in other diseases. To add to the confusion, blood tests can show high copper levels even when there is little copper in the tissues. These high copper levels may be due to injury, disease, or inflammation (23,25,26).

Because copper is needed to form new blood vessels, one group of researchers used a copper-lowering drug to find out if it helped patients with advanced kidney cancer. Some patients' cancers stopped growing during the 6-month treatment period. A few people had low white blood counts during treatment, requiring that treatment be stopped until they recovered. This was a small study, and further research is needed to find out if it can help more people with advanced cancer (27).

Another study measured copper levels in the blood of people who died from heart disease, and noted that their levels were high (28). It is not known whether the lab testing truly reflected copper levels in the body tissues, or exactly what caused the high levels. In contrast, a recent study gave copper supplements to healthy women with no signs

of copper deficiency. Their cholesterol and triglyceride levels improved, as did some other markers of heart disease risk. This small study did not look at actual heart disease, however. Further research is required to see if copper can affect heart disease risk (28,29, 30).

In others studies, serum levels of copper showed gradual increase from precancer to the cancer group (oral squamous cell carcinomas) as compared to normal subjects, which was statistically significant. (31,32)

References

- 1-Edwards, CRW., Bouchier, IA., Chilvers, E. Principle & practice of medicine. 17th edition. Churchill Livingstone. 1995.
- 2-Cavdar AO., Babcan E., Erton, J. Zinc deficiency in Hodgkin's diseases. *Europ. J. Cancer.* 1980;16:317-321.
- 3-Majeed TS., Al-Timimi, DJ., Al-Naimi A. Copper & zinc in malignant lymphoma. *J. Fac. Med. Baghdad.* 1992;34 (1): 51-57.
- 4-Wahbi SD, Al-Alawi, AF. Saeed Tk. Serum copper & ceruloplasmin in breast cancer. *Ann. Coll. Med. Mosul.* 1990;16:59-66.
- 5-Bucher, WC., Jones, SE. Serum copper & zinc ratio in patients with malignant lymphoma. *Am. J. Clin. Path.* 1977;68: 104-5.
- 6-Yousuf RM., Marbut MM., Al-jibouri SM. A study of selenium concentration in blood of ALL patients. *TMJ.* 1998;4:144-6.
- 7-Cohen Y., Epelbaum R., Haim N. The value of serum copper levels in non-Hodgkin's lymphoma. *Cancer.* 1984;53:296-300.
- 8-Babior B., Kipnes, R., Curnutte EJ. The production of superoxides by leukocytes. *J. Clin. Invest.* 1973; 52: 741-45.
- 9-Margalith, EJ; Schenker, JG. Copper and zinc levels in normal and malignant tissues. *Cancer.* 1983;52:868-872.
- 10-Fortes C., Forastere F., The immune effect of zinc & vitamin A supplementation on immune response in older population. *J. Am. Geriatr. Soc.* 1998;46:19-26.
- 11-Girodon F., Lombard M., Galan. P. Effect of micronutrient supplement on infection in elderly subjects. *Ann. Nutr. Metab.* 1997; 41:98-107.
- 12-Macknin MI., Zinc lozenges for common cold. *Cleveland Clin. J. Med.* 1999;66:27-32.
- 13-Scott M. Koski, K. Zinc deficiency impairs immune responses against parasitic nematode infections at intestinal . *J. Nutr.* 2000;1412S-1420s.
- 14-Shanker A. Prasad A. Zinc & immune function: The biological basis ed resistance to infection. *Am.J. Clin. Nutr.* 1998;68:447S-463S.
- 15-Kadir, MA, Amin, ST., Abdullah, NI. Determination of concentration of some trace elements in normal & pathological conditions. *Tikrit Medical Journal.* 2001; 7(2):54-7.
- 16-Chandra, RK. Excessive intake of zinc improve immune response. *JAMA.* 1984; 252:1443-6.
- 17-Hrgovic, M., Tesser., CF., Ninckler, TM., Tayler, GH. Serum copper levels in Lymphoma; special references to Hodgkin's disease. *Cancer.* 1968;21:743-755.
- 18-Araya M, Olivares M, Pizarro F, et al. Supplementing copper at the upper level of the adult dietary recommended intake induces detectable but transient changes in healthy adults. *J. Nutr.* 2005;135:2367-2371.
- 19-Bugel S, Harper A, Rock E, et al. Effect of copper supplementation on indices of copper status and certain CVD risk markers in young healthy women. *Br. J. Nutr.* 2005;94:231-236.
- 20-DiSilvestro RA, Sakamoto K, Milner JA. No effects of low copper intake on rat mammary tissue superoxide dismutase 1 activity and mammary chemical carcinogenesis. *Nutr Cancer.* 1998;31:218-220.
- 21-Finefrock AE, Bush AI, Doraiswamy PM. Current status of metals as therapeutic targets in Alzheimer's disease. *J Am Geriatr Soc.* 2003;51:1143-1148.
- 22-Kelley DS, Daudu PA, Taylor PC, et al. Effects of low-copper diets on human

- immune response. Am J Clin Nutr. 1995;62:412-416.
- 23-Ford ES. Serum copper concentration and coronary heart disease among US adults. Am J Epidemiol. 2000;151:1182-1188.
- 24-Martin-Lagos F, Navarro-Alarcon M, Terres-Martos C, Lopez-G de la Serrana H, Lopez-Martinez MC. Serum copper and zinc concentrations in serum from patients with cancer and cardiovascular disease. Sci Total Environ. 1997;204:27-35.
- 25-Percival SS. Copper and immunity. Am J Clin Nutr. 1998;67 (suppl. 5): 1064S-1068S.
- 26-Redman BG, Esper P, Pan Q, et al. Phase II trial of tetrathiomolybdate in patients with advanced kidney cancer. Clin. Cancer Res. 2003;9:1666-1672.
- 27-Renault E, Deschatrette J. Alterations of rat hepatoma cell genomes induced by copper deficiency. Nutr Cancer. 1997;29:242-247.
- 28-Strain JJ. Putative role of dietary trace elements in coronary heart disease and cancer. Br J Biomed Sci. 1994;51:241-251.
- 29-Wu T, Sempos CT, Freudenheim JL, Muti P, Smit E. Serum iron, copper and zinc concentrations and risk of cancer mortality in US adults. Ann. Epidemiol. 2004;14:195-201.
- 30-Ahmed MA., Al-Qubeessi, KB. The evaluation of trace elements in Idiopathic dilated cardiomyopathy. Tikrit Med. J. 2007; 13(2): 151-55.
- 31-Jaydeep, A. Serum levels of copper, zinc, iron and ceruloplasmin in oral leukoplakia and Squamous cell carcinoma. J Exp Clin Cancer Res. 1997; 16:3.
- 32-Varghese,, Sugathan, CK; Balsubramaniyan, G; Vijayakumar, T. Serum copper and zinc levels in premalignant or malignant lesions of oral cavity. Oncology. 1987;44:224-227.

Table (1): The mean, SD, & range of plasma copper (ug/ml) & plasma zinc (ug/ml) concentrations in healthy & ALL patients.

Elements	Mean $\pm$ S.D	Range
<i>A-zinc</i>		
Patients	6.39 $\pm$ 0.49	5.584 – 7.293
Control	7.195 $\pm$ 0.48	6.568 – 8.088
<i>B-Copper</i>		
Patients	1.568 $\pm$ 0.18	1.103 – 1.879
Control	1.367 $\pm$ 0.19	0.931 – 1.774