



Serum Copper, Zinc and Magnesium Levels in Children with Various Malignant Disorders

Çocuklarda Çeşitli Malign Hastalıklarda Serumdaki Bakır, Çinko ve Magnezyum Seviyeleri

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ABSTRACT

Purpose: The minute amounts of several trace elements including copper, zinc and magnesium play some roles as essential constituents of various biological organs. The serum concentrations these elements are modified in some malignancies. The aim of this study is to investigate the copper, zinc and magnesium levels in the serum of children with various malignant disorders.

Material and Methods: The serum levels of copper, zinc and magnesium were measured in 82 children with various malignant disorders and in 21 age-matched healthy controls using an atomic absorption spectrophotometer.

Results: The serum Cu, Zn and Mg concentrations were significantly higher than matched control values among patients with acute lymphoblastic leukemia (ALL) ($p<0.05$, $p<0.05$, $p<0.0001$, respectively) on the other hand, the serum Mg concentrations were also significantly higher than matched control values among patients with acute nonlymphocytic leukemia (ANLL) and other solid tumors ($p<0.0001$, $p<0.0001$, respectively) whereas there were no significant differences in serum Cu and Zn concentrations between healthy controls and in patients ANLL and other solid tumors. ($p<0.05$, $p<0.05$) Additionally the copper /zinc ratio in patients with acute lymphoblastic leukemia was significantly higher than the control value whereas a nonsignificant difference was found between healthy controls and patients with ANLL and other solid tumors.

Conclusion: Trace elements particularly copper and magnesium appear to be elevated in malignant diseases. Such elevation may prove to be useful markers to screen for and perhaps monitor relapse of malignant disease.

Key words: Copper, Zinc, Magnesium, Leukemia, Solid tumor, Copper/Zinc ratio

ÖZET

Amaç: Bakır, çinko, magnezyum dahil olmak üzere birçok iz elementlerin küçük miktarları dahi birçok biyolojik organların temel bileşenleri olarak rol oynamaktadır. Bu elementlerin serum konsantrasyonları bazı malign durumlarda değişiklik gösterirler. Bu çalışmanın amacı, çeşitli malign hastalığı olan çocukların serumlarındaki bakır, çinko ve magnezyum düzeylerini araştırmaktır.

Materyal ve Metod: Çeşitli malign hastalıklara sahip 82 çocuğun ve kontrol grubunu oluşturan yaş olarak denk 21 sağlıklı çocuğun bakır, çinko ve magnezyum düzeyleri atomik absorpsiyon spektrofotometre kullanılarak ölçüldü.

Bulgular: Akut lenfoblastik lösemili hastalarda ki (ALL) serum Cu, Zn ve Mg konsantrasyonları ($p<0.05$, $p<0.05$, $p<0.0001$) kontrol grubuna göre daha yüksek bulunmuştur. Diğer yandan, serum magnezyum konsantrasyonlarının akut nonlenfositik lösemide (ANLL) ve solid tümörlerde ($p<0.0001$, $p<0.0001$) kontrol grubuna oranla daha yüksek olduğu gözlenmiştir. ANLL hastalarında ve diğer solid tümörlerdeki ($p<0.005$, $p<0.05$) serum bakır ve çinko konsantrasyonları

ile kontrol grubu arasında önemli bir fark gözlenmemiştir. Ek olarak, ALL hastalarındaki bakır/çinko oranı kontrol grubuna göre daha yüksektir fakat kontroller ile ANLL ve diğer solid tümörler arasında herhangi bir fark gözlenmemiştir.

Sonuç: Malign hastalıklarda özellikle bakır ve magnezyum konsantrasyonunda bir artış bulunmuştur. Bu artışlar malign hastalıkların izlenmesi ve tekrarının takip edilmesi için yararlı belirteçler olabilir.

Anahtar Kelimeler: Bakır, Çinko, Magnezyum, Lösemi, Solid Tümör, Bakır/Çinko Oranı

INTRODUCTION

The minute amounts of several trace elements play some roles as essential constituents of various biological organs¹. Among these trace elements; copper (Cu) , zinc (Zn) and magnesium (Mg) have been the subject of a various disease

processes²⁻⁴. Since 1950, Zn and Cu levels in patients with malignant diseases have been extensively studied to see if they might serve as additional markers of cancerous activity^{5,6}. The serum concentrations of Cu, Zn and Mg are modified in some malignancies and some authors have demonstrated that serum Cu and Mg concentrations appear to be increased in certain forms of leukemia^{3-5,7-9}. As a result of these studies, it has been suggested that alterations in serum Cu levels and the zinc/copper ratio may serve as a prognostic marker^{6,10}. The purpose of this study is to investigate the Cu, Zn and Mg levels in the serum of children with acute lymphoblastic leukemia (ALL) , acute nonlymphocytic leukemia (ANLL) and other solid tumor cases and to compare them with healthy controls .

MATERIALS and METHODS

Eighty-two children with ALL, ANLL and solid tumors admitted to the pediatric hematology-oncology clinic and 21 healthy children followed in the outpatient clinics of our University Hospital were included in the study. Institutional Ethics Committee approved the study. The children under investigation were divided into four groups;

- Group I: Thirty-seven children aged 2-14 years with ALL
- Group II: Eleven children aged 3-14 years with ANLL
- Group III: Thirteen children aged 2-14 years with a variety of solid tumors
- Group IV (control group): Twenty-one healthy children aged 2-14 years

Venous blood samples were taken into deionised tubes at the time of diagnosis in all study participants. The blood samples were allowed to clot retraction over 60 minutes period and centrifuged at 2500 rpm for 30 minutes. The serum was removed and then stored at -20 °C in polystyrene tubes until final analysis. Serum Cu , Zn and Mg levels were determined by atomic absorption spectrophotometer using the Perkin – Elmer Model 2380⁴. Statistical analyses were done by Newman – Keuls test and variance analyses (Anova).

RESULTS

The mean serum Cu, Zn and Mg levels of various malignant conditions (Group I,II and III) age-matched control group (Group IV) are given in Table 1. The mean Cu, Zn and Mg levels were showed in table 1 for each group. As shown in Table 2 the serum Cu levels were significantly higher than control values in patients with ALL ($p < 0.05$), whereas a nonsignificant differences were observed for patients with ANLL and solid tumors versus controls. The serum Zn levels in patients with ALL were significantly higher than the control group (Table 3).

Table 1: The mean serum Cu ,Zn and Mg levels for various malignant conditions and healthy controls.

Groups	Serum Cu Conc. x±SD (µG/dl)	Serum Zn Conc. x±SD (µG/dl)	Serum Mg Conc. x±SD (mg/dl)
Group I n=37	163.42±58.04	132.70±51.25	2.09±0.42
Group II n=11	143.06±33.71	97.89±40.82	2.27±0.32
Group III n=13	142.92±61.44	115.21±35.30	2.24±0.36
Group IV n=21	132.63±26.44	107.59±21.29	1.68±0.20

Table 2: The serum Cu levels for various malignant conditions and healthy controls.

	Group I (ALL) N=37	Group II (ANLL) N=11	Group III (Solid tumor) N=13	Group IV (control) N=21	P<0.05
Serum Cu concentration (µ/dl)	163.42±58.04	143.06±33.71	142.92±61.44	132.63±26.44	I>IV

Table 3: The serum Zn levels for various malignant conditions and healthy controls.

	Group I (ALL) N=37	Group II (ANLL) N=11	Group III (Solid tumor) N=13	Group IV (control) N=21	Statistical difference
Serum Zn concentration (µ/dl)	132.70±51.25	97.89±40.82	115.21±35.30	107.59±21.29	I>IV

p<0.05

As can be clearly seen the serum Mg levels of all patient with malignant disorders were significantly higher than the healthy control group (Table 4) (p<0.0001, p<0.0001, and p<0.0001). The copper /zinc ratio was also calculated for all

malignant conditions and illustrated in Table 5. The ratio was significantly higher than control values in patients with ALL (p<0.01). A nonsignificant difference according to control was observed in patients with ANLL and solid tumors.

Table 4 : The Mg levels for various malignant conditions and healthy controls.

	Group I (ALL) N=37	Group II (ANLL) N=11	Group III (Solid tumor) N=13	Group IV (control) N=21	Statistical difference
Serum Mg concentration (mg/dl)	2.09±0.42	2.27±0.32	2.24±0.36	1.68±0.20	I>IV

Table 5: Serum Cu /Zn ratio for various malignant conditions and healthy controls.

	Group I (ALL) N=37	Group II (ANLL) N=11	Group III (Solid tumor) N=13	Group IV (control) N=21	Statistical difference
Serum Cu/Zn ratio	1.74±0.65	1.68±0.72	1.31±0.30	1.21±0.31	I>IV (p<0.01)

DISCUSSION

Trace elements play an important role in biological function. A number of studies have also looked at their role in malignant diseases. Among these studies, Zn and Cu have been the most extensively investigated trace elements²⁻⁴. Zinc is essential for DNA polymerase activity and is an integral part of rapid cell proliferation encountered in enlarging tumors¹¹. Copper is a component of many enzymes such as monoamine oxidase and superoxide dismutase. Such enzymes are key to ongoing cell activity². Most studies examining Cu levels in neoplastic diseases have demonstrated elevated levels^{5,6}. Zinc levels have shown a greater degree of variation. Most studies in malignancy indicate low levels, however, some remain in the normal range. When levels were noted to be low, they were often associated with abnormal humoral and cellular immunity^{6,9}.

In the present study, variable Zn levels were found among the various study groups. No statistically significant difference was notable when comparing malignant disease subgroups (Group I,II,III) with normal controls (Group IV). Serum Cu levels however were consistently elevated in the disease subgroups versus controls. Such findings are in agreement with previous studies⁷. The only statistically significant difference, however, was noted in the ALL versus control group (p<0.001). This result conflicts with previous reports, which have generally shown increased Cu levels in solid tumor and lymphoma patients rather than patients with ALL.

Examination of Mg levels indicated significantly higher levels in all disease groups compared with matched controls. These results

were also duplicated in one previous study published from Turkey³. All other studies have failed to reveal such findings¹². Higher levels of Mg may be a significant marker of malignant disease process and useful for screening and monitoring purposes. Further studies are needed to confirm this postulate.

As stated previously, determination of the serum copper /zinc ratio is a potentially useful prognostic aid in malignant disease and may prove useful in monitoring the response to treatment. In the present study copper /zinc ratio was significantly different when comparing the ALL and control group (p<0.01). The other groups failed to show significant difference when matched with controls. Overall, it appears that absolute Cu level is a more important guide to monitoring malignant disease than the copper /zinc ratio.

In conclusion trace elements particularly Mg and Cu appear to be elevated in malignant diseases. Such elevation may prove to be useful markers to screen for and perhaps monitor relapse of malignant disease. More extensive studies are encouraged to further explore and confirm these findings.

Conflict of interest statement: The authors declare no conflicts of interest.

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