SERUM ZINC, COPPER AND MAGNESIUM IN PATIENTS WITH BRAIN TUMOR

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Abstract:

Background: Trace elements such as copper (Cu), zinc (Zn), and magnesium (Mg) have an important chemical and biological roles. Recently different modes of changes in their concentrations have been shown to be correlated with the prognosis in selected human malignancies including brain tumor.

Materials and Methods: Ninety three individuals were included in the present study, 28 with benign brain tumor, 31 with malignant brain tumors, and 34 normal healthy controls. Serum Cu, Zn, and Mg were determined before surgical removal of the tumor and one week after the operation using the atomic absorption spectroscopy.

Results: Results of this study revealed that serum copper was markedly elevated ($p<0.05$) in malignant brain tumor patients followed by benign tumor patients. There is a significant difference in serum zinc in malignant brain tumor cases as compared with healthy controls. Serum magnesium in benign brain tumor patients was significantly different as compared with either control or malignant brain tumor. The surgical removal of the tumors lead to decrease serum copper and increase serum zinc as compared with their base level before surgery and they were directed to be within the normal ranges of the healthy control.

Conclusion: There is a different change in the level of trace elements in serum of brain tumor patients as compared with control and also before and after surgery. Further investigation needed to estimate the accurate causes of these changes.

Keywords: Zinc, Copper, Magnesium, Brain tumor, Cancer, Trace elements

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Introduction

Although the mineral elements constitute relatively small amounts of total body tissues, they are essential to many vital processes. Hence, the study of the level of some important trace elements in different disease is the field of extensive studies in recent years[1-2].

In malignant tumors, the estimation of trace elements level in different body tissue may give different profiles depending on the type and location of cancer[3-4]. Serum copper for example was markedly elevated in bronchial carcinoma; while serum zinc was significantly reduced compared with healthy control[5]. Timer *et al* found that zinc partly inhibited the metastasis of lung carcinoma[6]. A plasma copper was slightly increased in benign breast cancer and significantly increased in malignant breast cancer as compared with control group, while zinc level in all groups was not statistically significant[7].

There is important role of zinc, copper and magnesium in the development of normal brain function. There is a link between severely deregulated metal-ion homeostasis and the selective neuronal pathology[8]. Copper is a constituent of dopamine-beta hydroxylase, the critical enzyme in a catecholamine biosynthesis pathway[9]. Angiogenesis (new blood vessel growth) is very important process for the tumor growth and a sufficient level of copper appears to be required for angiogenesis and also many angiogenesis promoters appear to be dependant upon copper level[10]. Synthesis of serotonin which is necessary for melatonin synthesis involves zinc enzymes; zinc deficiency may result in low level of both hormones[11]. Zinc deficiency in injured brain causes a profound gliosis in the area surrounding the lesion, along with a severe damage to neuron[12].

A number of studies have demonstrated that the neurological motor and cognitive deficits induced by traumatic brain injury can be attenuated with administration of magnesium salt[13]. Magnesium is very necessary for the production of energy released by the ATP hydrolysis which significantly reduced in many diseases[14].

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From all of the above importance of these three elements in the brain functions and diseases we have measured the serum level of zinc, copper and magnesium in patients with different brain tumors either benign or malignant and also the level of these metals were measured after surgical interferences as possible tools for the follow up of the patients status.

Subjects & methods

Patients:

Blood samples were drawn from 59 patients with different brain tumor referred to the universal hospital of Iraqi college of medicine for surgical intervention. The patients with benign tumors were 28 patients (17 patients with meningioma, 7 patients with schwanoma, and 4 patients with dorsal neurofibroma). The tumor in these patients is removed totally by surgery. Patients with malignant tumors were 31 cases (16 patients with glioma, 6 patients with glioblastoma, 4 patients with medullary blastoma, 5 patients with brain metastases from breast and lung carcinoma). 34 healthy peoples were taken as control.

Venous blood samples were collected before initiating the operation, and seven days after operation .Sera were separated and kept at (-20ºC) until analysis.

Assay: 0.1ml of serum diluted to total volume of 1ml using 6% n-butanol solution analyzed for their copper and zinc contents using atomic absorption spectrophotometer (Schimadzu AA-646). Copper and zinc hallow cathode lamps were used at wavelengths of 324.75 nm and 213.9 nm respectively. The assay for magnesium estimation was carried out by adding 4.9 ml. of (1% Lanthanum chloride) solution to 0.1 ml. of serum. These solutions were aspirated directly into air-acetylene flame and the magnesium hallow cathode lamp were used at wavelength 285.2 nm.

Statistical methods

The results were analyzed statistically, and values were expressed as (mean ± standard deviation). The level of significance was determined by employing (t-test). Only when the (p) value was less than 0.05 was the difference between two groups considered statistically significant.

Results & Discussion

The mean and standard deviation values of serum copper of healthy controls and patients with brain tumor are presented in Table 1. Results of the patients with benign and malignant brain tumors before and after surgical removal of the tumors are also recorded. There is a significant increase ($p<0.05$) in serum copper of patients with benign and malignant tumors in comparison with healthy controls. While there is no significant difference between the patients with malignant and benign brain tumors. These results can be explained by considering the fact of angiogenesis process in the two types of tumors. The rapid cell division process requires a suitable blood supply and the angiogenesis process is very important and very active in the brain tumor tissue[10]. It reported that copper is very necessary to this process[10]. Copper which is important in the development of the brain[15] and is also involved in many neurological diseases[16,17] is transported in serum bound initially to albumin and later more firmly bound to cerruloplasmin where it is exchanged in the cupric form[18]. Cerruloplasmin is one of the acute phase reactant proteins which increased in acute inflammation and in neoplastic diseases[19] leading to increase the copper in serum of the patients with brain tumors. Some workers[10,20] used chelating agent therapy to reduce copper in animal tumor models. They found that the decrease in blood copper leads to stabilize tumor growth and the results also found to be encouraging in human patients with a variety of advanced and metastatic malignancies[10,20]. Yoshida *et al*[4] found that metastatic carcinoma and malignant gliomas revealed significantly higher tissue copper concentration than tissue of control and maningiomas.

Serum copper was significantly higher in metastatic carcinoma group than control. Serum copper is significantly decreased ($p<0.05$) after surgical removal of tumors. The benign tumors were totally removed while the malignant tumors were partially removed. This may be due to the fact that, after one week of operation the inflammatory response would be reduced and hence the level of acute phase reactant proteins (including cerruloplasmin) tend to be within normal range.

Table 1: Serum copper in healthy controls and patients with brain tunors

Parameter	S. Copper Mean±SD µmol/L	Compared Groups	P value
Healthy Controls	21.4±6.2	Benign Vs control	0.0095
Benign:			
Before surgery	27.2±9.1	Before Vs after surgery	0.0003
After surgery	22.9±7.9	Malignant Vs control	0.0210
Malignant:			0.0456
Before surgery	33.1±9.4	Before Vs after surgery	
After surgery	24.1±9.2	Benign Vs malignant (before surgery)	0.8760

Table 2 showed that the serum level of zinc is not changed in the patients with benign brain tumors as compared with controls. Also there is no change in serum zinc after removal of benign tumors .This has been seen in other types of tumors such as benign breast cancer[21]. The results revealed that there is a significant decrease between malignant brain tumors as compared with either control and benign brain tumor. These results indicate that the change in serum zinc is involved in the malignant tumors as shown by different workers who studied the malignant tumors in different organs[22].

The partial removal of the malignant brain tumor leads to maintain normal serum zinc level as compared with the serum zinc before surgery. This result confirms the concept of dependence of serum zinc level on the malignancy of tumor tissue. In addition to the fact that the rapid growth of cells requires an increase in the demand of cells to zinc and hence there is a decrease in serum zinc.

Table 2: Serum zinc in healthy controls and patients with brain tumors

Parameter	S. zinc Mean±SD µmol/L	Compared Groups	P value
Healthy Controls	16.9±2.7	Benign Vs control	0.03426
Benign:			
Before surgery	12.4±3.9	Before Vs after surgery	0.8964
After surgery	13.6±6.6	Malignant Vs control	0.000006
Malignant:			
Before surgery	9.5±3.8	Before Vs after surgery	0.01232
After surgery	15.4±7.3	Benign Vs malignant (before surgery)	0.00543

Serum magnesium in benign, malignant, and controls are shown in Table 3. The results have revealed that there is a significant difference between both benign and malignant brain tumors as compared with healthy controls. There is a significant difference between serum magnesium in malignant and benign groups'. Also the surgery has no effect on the serum magnesium after one week of operation.

Table 3: Serum magnesium in healthy controls and patients with brain tumors

Parameter	S. zinc Mean±SD µmol/L	Compared Groups	P value
Healthy Controls	2.28±0.49	Benign Vs control	0.00087
Benign:			
Before surgery	1.78±0.62	Before Vs after surgery	0.87210
After surgery	2.06±0.43	Malignant Vs control	0.986744
Malignant:			
Before surgery	2.02±0.54	Before Vs after surgery	0.03589
After surgery	2.15±0.47	Benign Vs malignant (before surgery)	0.045369

In cellular systems, magnesium is a second most abundant element and is involved in basically all metabolic pathways[22]. Magnesium is very necessary for the cell metabolism and production of energy released by the ATP hydrolysis which is significantly reduced in brain in many diseases[14]. Hence the change in serum magnesium is significant in the uncontrolled production state either benign or malignant tumors as compared with controls.

Conclusions

Brain tumors are associated with various changes in the serum concentration of copper, zinc, and magnesium. Serum zinc was increased and serum copper was decreased after surgical removal of the tumor.

Recommendations

Study of trace elements in brain tumor patients are required using a higher number of cases. In addition to study serum trace elements at different intervals after operation to estimate the accurate causes of the changes in these parameters.

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