

Examination of preoperative and postoperative levels of rare earth elements (Zn, Cu, Mg, Pb, Mn, Cd, Co and Fe) in the blood of ovarian cancer patients

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Abstract

Objective: In this study, serum material drawn preoperatively and postoperatively from totally 33 patients who applied to Department of Gynaecology of Yüzüncü Yıl University Faculty of Medicine and Van Training and Research Hospital due to suffering from ovarian cancer was used.

Material and Methods: The serum levels (Zn, Cu, Mg, Pb, Mn, Cd, Co and Fe) were determined by the method of Atomic Absorption Spectrophotometry at Spectrometer in Yüzüncü Yıl University Central Research Laboratory. The levels of rare-earth, trace and heavy elements were determined from the serum samples which were drawn from healthy and volunteer 30 women who were close to the same age group.

Results: This study found out a significant difference ($p < 0.001$) between the preoperative and postoperative levels of lead, manganese and iron in ovarian cancer patients. While a significant difference ($p > 0.005$) wasn't discovered between the preoperative and postoperative levels of zinc, copper, cadmium and cobalt in ovarian cancer patients, a statistically significant difference was found between the preoperative and postoperative levels of magnesium ($p = 0.07$) in those patients.

Conclusion: Consequently, Zn is important in the prognosis of the disease because it is a strong antioxidant element. The elements Mg, Mn and Fe can be significant markers for ovarian cancer and especially low level of Mn may increase the risk of ovarian cancer. Also, such elements as Zn, Cu, Mg, Pb, Mn, Cd, Co and Fe may play an important role in pathogenesis of ovarian cancer.

Keywords: Ovarian Cancer, Blood, Serum, Rare-earth Element, Heavy metals

Introduction

According to World Health Organization (WHO), there are three reasons behind such an increase in cancer cases as follows: smoking, increasing elderly population and obesity. Considering the data obtained from their studies, WHO put forwards that cancer cases will be the first and the most important reason of death across the world after the year 2015 [1,2] According to the data of Ministry of Health, approximately 175,000 people are diagnosed with cancer every year in Turkey. There isn't a statistically significant difference among regions in terms of cancer incidence. The number of deaths arising from cancer is increasingly growing in Turkey. For the last decade, the death rate has increased by 80%. Basing on the research conducted by the Turkish Statistical Institute [3,4,5,6], the rate of cancer-related deaths reached to 21% in 2012 whereas that rate was 12% in 2002. The incidence of cancer-related deaths and cancer cases in Turkey increases by the rates similar and parallel to those seen across the world. Apart from those reasons, the fact that the previously-unknown cancer cases have been

found out and cancer recording has been improved is another reason behind the increase in cancer statistics. Considering the data obtained by World Health Organization [1,2], the cancer incidence in Turkey is lower than those seen in the countries of America and Europe. Ovarian cancer is increasingly posing a hazard for people lately. Ovarian cancer is highly seen among elderly women and most of the studies deal with aetiology of ovarian cancer because the primary goal should be finding out the different reasons of ovarian cancer.

It is essential to take rare-earth elements at certain rates to enable human organism to maintain its normal functions. These elements join the various structural and functional activities of organism and get involved especially in different enzyme systems and hence they play important roles for occurrence of living phenomena and survival [7]. It has been discovered by the studies on different types of cancer within literature that the levels of Zn, Mn, Cu, Mg and Fe sometimes increase and decrease [8,9,10,11]. There are a

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considerably limited number of researches regarding rare-earth elements on ovarian cancer.

In this study, the preoperative and postoperative levels of rare-earth elements (Zn, Cu, Mg, Pb, Mn, Cd, Co, Fe) in blood in ovarian cancer patients were examined.

Materials and Methods

Materials

Totally 33 patients who applied to Yüzüncü Yıl University Dursun Odabaşı Medical Center Gynaecology Unit and Van Training and Research Hospital Gynaecology Unit and were diagnosed with ovarian cancer were determined preoperatively and postoperatively between June 2013 and February 2014. Before collecting the blood samples in this research, the approval of Clinic and Laboratory Researches Local Ethics Committee of Van Training and Research Hospital was obtained. A control group consisting of 30 healthy and volunteer people was used in order to compare the results gained from the patient group in the study.

In our research, 3 ml blood was drawn from brachial vein of 33 patients, who were diagnosed with ovarian cancer, before operation and after one month following the operation. The drawn blood was centrifuged in venous biochemistry tube at Nüve NF 800 centrifuge at 5000 rpm for ten minutes and its serum was extracted. The serum was kept at -80°C until it was treated. When the adequate number of samples was obtained, the rare-earth elements in serum (Zn, Cu, Mg, Pb, Mn, Cd, Co and Fe) were determined by the method of Atomic Absorption Spectrophotometry at Spectrometer: M Series V1,23 in Yüzüncü Yıl University Central Research Laboratory.

Analysis Methods

Determining heavy metal, rare-earth elements and trace elements

Trace elements, mineral substances and metals (Zn, Cu, Mg, Pb, Mn, Cd, Co and Fe) were determined from serum samples by the method of Atomic Absorption Spectrophotometry.

Statistical Comments

Regarding the focused properties, the descriptive statistics were expressed as average, standard deviation, minimum and maximum value. In terms of these properties, one-way analysis of variance was performed in order to compare the group averages. Following the analysis of variance, Duncan Multiple Comparison - test was used to determine the different groups. For identifying the relation between these variables, Pearson correlation coefficients were calculated separately for each group. Statistical significance level was

taken as 5% ($p < 0.05$) in the calculations for which SPSS statistics package program was used.

Results

This study found out a significant difference ($p < 0.001$) between the preoperative and postoperative levels of lead, manganese and iron in ovarian cancer patients. While a significant difference ($p > 0.005$) wasn't discovered between the preoperative and postoperative levels of zinc, copper, cadmium and cobalt in ovarian cancer patients, a statistically significant difference was found between the preoperative and postoperative levels of magnesium ($p = 0.07$) in those patients.

Discussion

Ovarian cancer ranks the fourth among the cancer-related deaths after breast, lung and colon cancer [12]. Ovarian cancer leads to more deaths than the total number of all gynaecological malignance in the United States. 204,000 women are diagnosed with ovarian cancer and 125,000 of these women die because of it across the world every year (WHO). Except several particular early symptoms, there isn't an efficient screening test for ovarian cancer. Consequently, $\frac{3}{4}$ of the patients are at advanced stage of cancer when they are diagnosed. In a research conducted on the patients undergoing chemotherapy in Finland, it was discovered that the patients taking selenium and vitamin E supplement respond to treatment better [13]. A study which compared the serum Cu/Zn levels in healthy and gynaecological tumour cases found out that the serum Cu/Zn levels help following up the course of disease [14]. There are several studies which put forwards that there is a relation between trace element level and progress of hepatocellular carcinoma. In those studies, the levels of serum, copper, iron and zinc were been found low in liver cancer patients [15].

A research conducted in China revealed that the activity of superoxide dismutase enzyme was low in the patients with hepatocellular carcinoma. The fact that Zn and Cu levels were found low in the same patient group was associated to low enzyme activity. In a study on colon cancer in the literature, Zn level was found higher compared to those of healthy people [10]. A research discovered that Zn level in lung cancer patients was significantly lower than those of healthy control group [8]. Likewise, a study revealed that Zn level in prostate cancer patients was significantly lower than those of healthy control group [11]. This study found out that Zn level in ovarian cancer patients was found higher in preoperative group compared to those of control and postoperative group; but there was no statistical significance ($p = 0.160$).

Table 1. The findings regarding ovarian cancer patients, postoperative and healthy control group

Parameter	Control n=30 X±Sx	Preoperative Ovarian Cancer n=33 X±Sx	Postoperative Ovarian cancer n=33 X±Sx	p Value
Zn (mg/L)	0.863±0.277	0.875±0.307	0.745±0.288	0.160
Cu (mg/L)	1.200±0.299	1.185±0.363	1.085±0.343	0.322
Mg (mg/L)	28.435±2.952	29.866±4.976	25.760±6.537	0.007
Pb (mg/L)	0.157±0.113 ^a	0.206±0.118*	0.352±0.201 ^b	0.001
Mn (mg/L)	0.107±0.023 ^a	0.064±0.025*	0.093±0.023 ^b	0.001
Cd (mg/L)	0.030±0.249	0.069±0.115	0.060±0.043	0.095
Co (mg/L)	0.268±0.082	0.254±0.120	0.316±0.168	0.146
Fe (mg/L)	1.812±0.438 ^a	0.491±0.136*	1.050±0.571 ^b	0.001

1: difference between a and b is significant. (p<0.05)

2: difference between a and * is significant. (p<0.05)

3: difference between b and * is significant. (p<0.05)

Table 2. Correlation coefficients for control group

	Zn	Cu	Mg	Pb	Mn	Cd	Co	Fe
Zn	1							
Cu	0.195	1						
Mg	0.427*	0.439*	1					
Pb	0.076	0.279	0.341	1				
Mn	-0.080	-0.105	0.140	-0.109	1			
Cd	0.212	0.345	0.403*	0.778**	-0.202	1		
Co	0.052	0.139	0.181	0.616**	-0.232	0.585**	1	
Fe	-0.345	-0.248	0.004	-0.036	0.272	-0.242	-0.126	1

* p<0.05 ; ** p<0.01

Mg level: There is positive correlation with Zn and Cu.

Cd level: There is a positive correlation with Mg and Pb.

Co level: There is positive correlation with Pb and Cd.

Table 3. Preoperative correlation coefficients for patient group

	Zn	Cu	Mg	Pb	Mn	Cd	Co	Fe
Zn	1							
Cu	0.103	1						
Mg	0.549**	0.201	1					
Pb	0.239	0.120	0.270	1				
Mn	0.117	0.346*	0.429*	0.184	1			
Cd	0.028	-0.076	0.195	0.410*	0.210	1		
Co	0.246	-0.085	0.555**	0.335	0.539**	0.460**	1	
Fe	0.085	0.302	0.125	0.335	0.389*	-0.047	0.147	1

Mg level: There is positive correlation with Zn.

Mn level: There is positive correlation with Cu and Mg.

Cd level: There is positive correlation with Pb.

Co level: There is positive correlation with Mg, Mn and Cd.

Fe level: There is positive correlation with Mn.

Table 4. Correlation coefficients for postoperative group

	Zn	Cu	Mg	Pb	Mn	Cd	Co	Fe
Zn	1							
Cu	0.268	1						
Mg	0.491**	0.702**	1					
Pb	-0.218	0.244	0.439*	1				
Mn	0.072	0.297	0.398*	0.464**	1			
Cd	-0.104	0.207	0.421*	0.906**	0.482**	1		
Co	-0.179	0.240	0.505**	0.805**	0.442*	0.871**	1	
Fe	0.436*	-0.216	-0.177	-0.538**	-0.165	-0.514**	-0.551**	1

p<0.05 ; ** p<0.01

Mg level: There is positive correlation with Zn and Cu.

Pb level: There is positive correlation with Mg.

Mn level: There is positive correlation with Pb and Mg.

Cd level: There is positive correlation with Pb, Mg and Mn.

Co level: There is positive correlation with Mg, Pb, Mn and Cd.

Fe level: There is positive correlation with Zn and negative correlation with Pb, Cd and Co.

In a study, Cu level in colon cancer patients was found significantly higher compared to those of healthy control group [10]. A research on lung cancer discovered that Cu level was lower than those of healthy people [8]. This study revealed that Cu level in ovarian cancer patients was lower in preoperative group compared to control group and higher than those of postoperative group; but there was no statistically significance.

A research on colon cancer discovered that Mg level was higher than those of healthy people [10]. Mg level in lung cancer patients was found significantly lower than those of healthy control group in a study [8]. This study found out that Mg level in ovarian cancer patients was higher in the preoperative group than those of control and postoperative group and was statistically significant.

It was revealed by a study that Pb level in lung cancer patients was significantly higher than those of healthy control group [8]. Likewise, a research discovered that Pb level in kidney cancer patients was higher than those of healthy people [9]. It was presented by a study in Turkey that Pb level in renal cell carcinoma increased significantly compared to healthy people [16]. A literature on colon cancer found out that Pb level was higher than those of healthy people [10]. In this study, Pb level in ovarian cancer patients was found higher in the preoperative group compared to control group but lower than those of postoperative group and statistically significant.

Mn level was found higher than those of healthy people in a research regarding colon cancer [10]. A study discovered that Mn level in lung cancer patients was significantly higher than those of healthy control group [8]. Likewise, it was revealed by a research that Mn level in prostate cancer patients was significantly higher than those of healthy control group [11]. This study revealed that Mn level in ovarian cancer patients was lower in the preoperative group than those of control and postoperative group and statistically significant.

A study found out that Cd level in lung cancer patients was significantly higher compared to those of healthy control group [8]. It was discovered by a literature on kidney cancer patients that Cd level was higher than those of healthy people [9]. A study on colon cancer revealed that Cd level was higher than those of healthy people [10]. It was presented by a study in Turkey that Cd level in renal cell carcinoma increased significantly compared to healthy people [16]. A study compared Cd levels of glioma cancer patients and healthy people and presented that Cd level in glioma patients was significantly higher [17]. This study found out that Cd level in ovarian cancer patients was higher in the preoperative group compared to those of control and postoperative group and a result close to statistically significance was obtained.

Co level in lung cancer patients was found significantly higher than those of healthy control group in a research [8]. In this study, it was discovered that Co level in ovarian cancer patients was lower in the preoperative group compared to those of control and postoperative group and there was no statistically significance.

A study revealed that Fe level in lung cancer patients was significantly higher than those of healthy control group [8]. In a research, Fe level decreased in prostate cancers [11]. This study presented that Fe level in ovarian cancer patients was found lower in preoperative group compared to those of control and postoperative group and there was statistically significant difference.

This study discovered that Mg level in control group had a positive correlation with Zn and Cu values while Cd level had a positive correlation with Mg and Pb. Also it was revealed that Co level had positive correlation with Pb and Cd. In preoperative group, Mg level was found to have positive correlation with Zn. A positive correlation was seen between Mn level and Cu and Mg. Also Cd level had a positive correlation with Pb. While Co level had positive correlation with Mg, Mn and Cd, Fe level had positive correlation with Mn. In postoperative group, Mg level had positive correlation with Zn and Cu. Pb level had positive correlation with Mg; Mn level with Pb and Mg; Cd level with Mg, Pb and Mn; Co level with Mg, Pb, Mn and Cd and Fe level with Zn. Fe level had negative correlation with Pb, Cd and Co.

Conclusion

In conclusion, Zn is important in the prognosis of the disease because it is a strong antioxidant element. Zn level was found high in some studies in literature while it was low in some of them. In our study, Zn level in ovarian cancer patients was found higher in preoperative group compared to control and postoperative group; but a statistically significance wasn't obtained. However, it can be stated that this result is compatible with the literature studies [8,10,11]. Likewise, the variations in the levels of Mg, Mn and Fe can be important markers for diagnosis and follow-up of ovarian cancer. Low serum Mn level can be related to ovarian cancer risk. According to these conclusions, such elements as Zn, Cu, Mg, Pb, Mn, Cd, Co and Fe can play an important role in pathogenesis of ovarian cancer. Due to low number of patients and local service of the hospital in our study, we consider it beneficial to conduct studies on wider areas and more patients. We are of the opinion that this study will provide an insight for the further studies to be performed in this field.

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