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Evaluation of serum zinc level as a risk factor for gastrointestinal cancers

Reza Khalili Dizaji[1], Babak Rashidian[1], Mohammad Bahadoram[2], Maedeh Barahman[3], Bayazid Ghaderi[4], Mohsen Rajabnia Chenari[1,5*]

[1]Department of Internal Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran
[2]Medical Student Research Committee and Social Determinant of Health Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
[3]Department of Radiation Oncology & Firoozgar Clinical Research Development Center, Iran University of Medical Sciences, Tehran, Iran
[4]Liver and Digestive Research Center, Kurdistan University of Medical Sciences, Sanandaj, Iran
[5]Student Research Committee, Kurdistan University of Medical Sciences, Sanandaj, Iran

***Correspondence to**
Mohsen Rajabnia-Chenari,
Email: Dr.Rajabnia@Outlook.com

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Abstract

Introduction: Gastric adenocarcinoma and esophageal squamous cell carcinoma (ESCC) are the second and third common cancer in Iran respectively and are the leading causes of cancer deaths in the world. The status of serum zinc level in these cancers has not been fully evaluated.
Objectives: The aim of the study was to compare serum zinc levels in patients with ESCC and gastric adenocarcinoma as compared to patients with other non-digestive cancers.
Patients and Methods: This cross-sectional study was conducted on 100 consecutive patients (10 patients with SCC of the esophagus, 40 patients with gastric adenocarcinoma and 50 cases with other non-digestive cancers as the controls). Morning blood samples were taken containing 5 ml of blood from both groups and immediately stored in the laboratory at 8°C until all samples were taken. After collecting, serum levels of zinc in the specimens were measured by 24i chemistry analyzer. The SPSS version 23.0 for Windows was used for the statistical analysis.
Results: The results of this study did not show a significant difference between mean serum level of zinc across the patients with ESCC and patients with gastric adenocarcinoma or those with other non-digestive cancers adjusted for age and gender ($P>0.05$). However, a significant difference between the mean serum zinc level in patients with gastric adenocarcinoma and other non-digestive cancers was detected ($P<0.05$).
Conclusion: Regarding the normal serum level of zinc in other non-digestive cancers and a decrease in zinc level in gastrointestinal cancers in our study, malnutrition which is common in all malignancies, has no effect on zinc deficiency in gastrointestinal malignancies, and zinc deficiency can be considered as a primary risk factor for the development of these two digestive malignancies.

Introduction

Gastric adenocarcinoma and esophageal squamous cell carcinoma (ESCC) are the second and third common cancer in Iran respectively (1) and are the leading causes of cancer deaths in the world (2). These cancers in Iran, especially esophageal cancer are more prevalent in northern Iran as compared with other parts of the world (1). Esophageal cancer is among the eight most common cancer in the world and is now considered as the sixth cause of death from cancer. The highest incidence of esophageal cancer in the world is in the region of the "esophageal cancer belt", which starts from Gonbad-Kavoos city in northeastern Iran and extends to the north of China. Type of squamous cell carcinoma (SCC) is the most common type of esophageal cancer in these areas (3). The type of squamous cell appears in this layer covering the esophagus, and

Key point

Regarding the normal serum level of zinc in other non-digestive cancers and a decrease in zinc level in gastrointestinal cancers in our study, malnutrition which is common in all malignancies, has no effect on zinc deficiency in gastrointestinal malignancies, and zinc deficiency can be considered as a primary risk factor for the development of these two digestive malignancies.

then develops in the esophagus. Approximately 60% of cases occur in the middle part of the esophagus (4). This malignancy is more common in men and appears mostly after the age of 50 years and is more common in societies with poor socioeconomic status (5). The most common type of gastric cancer is adenocarcinoma, the source of which is the gastric mucosal glands. This tumor often invades the stomach wall quickly. Although the esophageal SCC only contains one type of tumor, it differs with the degree of differentiation, while gastric adenocarcinoma has different types with different distinctions (6). There are several risk factors in both types of cancers that nutritional factors and some nutritional deficiencies are among the most important factors (7). A combination of external and internal factors is also associated with the onset and progression of cancers such as trace elements (8). Trace elements are among the basic constituents of biological processes, including oxidative processes. Oxidative processes play an important role in cancer development. Studies have been conducted on changes in serum levels of rare elements, especially copper and zinc in various cancers over the last few years. Zinc is one of the few rare elements that play a major role in many metabolic processes in the body, including in the building of 200 types of metalloenzyme and also in the production of antioxidant metallothionein (8-11). Several years ago, the role of zinc in delayed oxidative reactions has been known. Hence, the chronic deprivation of this element increases the susceptibility to some oxidative stress reactions. It has been shown that zinc can increase cellular growth inhibition and increase apoptosis. Cancer cell incubation with physiological levels of zinc has led to significant cell growth inhibition. Generally, the consequent of zinc activity in the body reduces the number of tumor cells and decreases tumor volume (12). The results of some studies showed a difference in the serum levels of zinc between the patients with gastrointestinal cancers and healthy individuals (13-16). According to the high prevalence of gastrointestinal cancers and the role of zinc in delaying oxidative reactions we intended to conduct a study on this subject.

Objectives

The aim of the present study was to compare the serum level of zinc in patients with SCC and gastric adenocarcinoma compared to patients with other non-digestive cancers.

Patients and Methods

Study population

This cross-sectional study was conducted on 100 consecutive patients hospitalized at different wards in Tohid hospital in Sanandaj city, Iran in 2015. In this study 10 patients with SCC of the esophagus, 40 patients with gastric adenocarcinoma and 50 cases with other non-digestive cancers as the controls were assessed before treatment. Exclusion criteria include the presence of other malignancies in patients with SCC and gastric adenocarcinoma and patients undergoing treatment prior to screening for serum level of zinc. Control subjects were matched with the cases groups in terms of demographic data (age and economic conditions). Morning blood samples were taken containing 5 mL of blood from both groups and immediately stored in the laboratory at 8°C until all samples were taken. After collecting, serum levels of zinc in the specimens were measured by 24i chemistry analyzer (Biorex Diagnostic kit).

Ethical issues

The research followed the tenets of the Declaration of Helsinki and its later amendments. Ethical considerations in this study included explaining the subject of research to individuals and obtaining written consent from them for the preparation of serum samples. Meanwhile, the subjects were assured that their information would be stored confidentially in information gathering forms and the results would be presented as a whole sample population. This research has approved by Kurdistan University of Medical Sciences.

Statistical analysis

Results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by absolute frequencies and percentages for categorical variables. Normality of data was analyzed using the Kolmogorov-Smirnoff test. Quantitative variables were also compared with *t* test or Mann-Whitney U test. For the statistical analysis, the statistical software SPSS version 23.0 for Windows (SPSS Inc., Chicago, IL) was used. *P* values of 0.05 or less were considered statistically significant.

Results

The total number of patients studied was 100 patients aged 18 to 90 years and mean age of 57.13 years. Regarding the serum level of zinc, the highest and the lowest level was 140 mg/dL and 11 mg/dL respectively with a serum average of 73.16, mg/dL. The mean serum level of zinc in men and women with gastric adenocarcinoma was 66.46 ± 15.38 mg/dL and 69.69 ± 19.90 mg/dL respectively with no significant difference. Additionally, the mean level of zinc in men and women with ESCC was 65.38 ± 11.26 mg/dL and 64.12 ± 12.37 mg/dL respectively that was not able to statistical comparison due to the small number of samples. Mean serum zinc level in patients with other non-digestive cancers was 77.71 ± 26.35 mg/dL in men and 81.08 ± 18.96 mg/dL in women with no meaningful difference (Table 1). Regarding age group, the mean serum levels of zinc in patients with gastric adenocarcinomas was 79.83 ± 19.52 mg/dL in the age group of 50 years and below and 65.62 ± 15.81 mg/dL in older individuals with no difference. Furthermore, the mean level of zinc in other non-digestive cancers in two age subgroups was 84.92 ± 17.90 mg/dL and 74.00 ± 25.75 mg/dL respectively with no significant difference (Table 2). Furthermore, the mean level of zinc in patients with gastric adenocarcinoma was 65.75 ± 16.93

Table 1. The mean serum level of zinc in patients with gastric adenocarcinoma and other non-digestive cancers adjusting gender

Type of cancer	Gender	Number	Mean level of zinc (mg/dL)	SD	*df*	T score	*P* value
Gastric adenocarcinoma							
	Male	24	66.46	15.38	38	-0.58	0.562
	Female	16	66.69	19.90			
Non-digestive cancers							
	Male	24	77.71	26.35	48	-0.52	0.640
	Female	26	81.08	18.96			

Table 2. The mean serum level of zinc in patients with gastric adenocarcinoma and other non-digestive cancers adjusting age groups

Type of cancer	Gender	Number	Mean level of zinc (mg/dL)	SD	*df*	T score	*P* value
Gastric adenocarcinoma							
	≥ 50 y	6	79.83	19.52	38	1.96	0.057
	< 50 y	34	65.62	15.81			
Non-digestive cancers							
	≥ 50 y	25	84.92	17.90	48	1.47	0.088
	< 50 y	25	74.00	25.75			

Table 3. The mean serum level of zinc in patients with gastric adenocarcinoma and other non-digestive cancers

Type of cancer	Number	Mean level of zinc (mg/dL)	SD	*df*	T score	*P* value
Gastric adenocarcinoma	40	67.75	16.93	88	-2.70	0.008
Non-digestive cancers	50	76.42	22.63			

mg/dL that was significantly lower than that revealed in those with other gastrointestinal cancers as 76.42 ± 22.63 mg/dL (Table 3).

Discussion

Zinc is known as an essential element in human, plant and animal nutrition and a part of 200 metalloenzymes essential for the function of the immune system, nerves, digestion, skin and the glands (17-19). Serum and plasma zinc concentrations in adults range from 80 to150 µg/dL. According to the results of this study, the mean serum zinc level in patients with SCC of the esophagus was lower than the gastric adenocarcinoma and the serum zinc level of these two types of cancer was lower in comparison to patients with other gastrointestinal cancers. In general, serum zinc was lower than standard serum zinc concentration. The results of this study regarding low levels of zinc in cancer patients were consistent with the findings of Cunzhi et al (20), Yaman et al (21) and Mazdak et al (22). Despite several studies that found low serum levels of zinc in cancer patients, other studies have reported contradictory results (23-25). One of the reasons for justifying this contradiction may be the measurement errors and interactions between these elements and also might be due to continuous fluctuations of these elements in the human body. Studies have shown that zinc is present in the chemical structure of antioxidant enzymes, such as superoxide dismutase. These enzymes protect cells from oxidation and degradation of DNA. Zinc deficiency in the body increases the cell's sensitivity to DNA degradation factors and disrupts host protective mechanisms against cancer (11,26).

Gender had no significant relationship with mean serum level of zinc. The mean serum level in men with gastric adenocarcinoma was higher than that in women. In non-digestive cancers, this average was higher in women than in men. Additionally, the mean level of zinc in patients aged lower than 50 years with gastric adenocarcinoma was higher than the younger individuals. Serum level of zinc was higher in patients with non-digestive cancers older than 50 years as compared to the younger, however this difference was not significant. In the studies by Tanir et al (27) and Demirkirap et al (28), age did not have an effect on the incidence of cancer, while in another study by Dehaven et al (29), the rate of cancer increased with age increasing. The mean serum zinc level in patients with gastric adenocarcinoma was lower than that in patients with other gastrointestinal cancers with a significant difference similar to the studies of Zhang et al study (13), Li et al (14).

Conclusion

Regarding the normal serum level of zinc in other non-digestive cancers and a decrease in zinc level in gastrointestinal cancers in our study, malnutrition which is common in all malignancies, has no effect on zinc deficiency in gastrointestinal malignancies, and zinc deficiency can be considered as a primary risk factor for the development of these two digestive malignancies.

Study limitation

This is a single center study. This study can be a pilot for larger investigation on this aspect of cancer patients.

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Authors' contributions

RKD, BG and MB helped in the design of study and preparation of final draft. MR and MB contributed to data analysis. BR helped in conducting the study, data collection and doing interview and data analysis. All authors read and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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