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The Comparison of Lead and Zinc Plasma Levels in Gastric Cancer Patients with Healthy Volunteers

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Abstract: Gastric cancer is common in developing countries. There are several risk factor as carcinogen for developing the cancer. Zinc and lead have important role in oxidative stress in cells.The aim of this study was determination of these elements level in the plasma of gastric cancer patients. Thirty two patients with gastric carcinoma diagnosis confirmed by pathological samples and 32 matched healthy volunteers included in the study. The levels of these elements were determined in the blood by atomic absorption. The zn plasma levels in patients and control group were found to be 1.49±0.75 and 2.12±0.83 mg L^{-1}, respectively ($p<0.01$). The plasma Pb level was found to be 0.76±0.18 mg L^{-1} in patients and 0.56±0.07 mg L^{-1} in control group ($p<0.001$). In this study, gastric cancer patients had a lower Zn level and a higher Pb level compared to healthy volunteers. With regard to critical role of trace elements as a risk factor for development of cancer, the consistency of our results would confirm the potential benefit of using Zn supplement and also the reducing of Pb for prevention of gastric cancer in high risk individual.

Key words: Zinc, lead, cancer, gastric, healthy volunteer

INTRODUCTION

Gastric cancer is the second most common cancer worldwide, with a frequency that varies greatly across different geographic location (Dicken *et al*., 2005). Gastric cancers are common in developing countries. In Iran, Gastric cancer was the most common malignancy in males (Shahraz *et al*., 2003). The incidence of gastric cancer rises with increasing age with the peak occurring predominantly between 50 and 70 and it is more common in men (male: female ratio 2:1) (Barr, 2007).

Despite the decreasing worldwide incidence, gastric cancer accounts for 3-10% of all cancer related death (Dicken *et al*., 2005). Ninety percent of gastric malignancies are adenocarcinoma (Dicken *et al*., 2005) and most of them locate distally to the cardia (distal gastric cancer) with a lower incidence in western countries (Jianguang and Hemminki, 2006). The site for development of carcinomas is changing, with tumors moving towards the gastro-esophageal junction and cardia. Carcinoma in the upper third now accounts for 39% of tumors compared with 17% only thirty year ago (Barr, 2007). The different time trends of distal and cardia cancers indicate different etiologies.

Zinc is considered the most abundant trace intracellular element and plays an important role in transcription factor function, antioxidant defense and DNA repair. Dietary deficiencies in zinc can contribute to single- and double-strand DNA breaks and oxidative modifications to DNA that increase risk for cancer development (Ho, 2004). Hypozincemia is a nonspecific observation and decreased serum zinc levels have been found in other diseases such as cirrhosis, hepatitis, lung infections and some other cancers (Schwartz, 1975). Zinc deficiency can occur in populations with low dietary zinc intake and high concentration of phytate, a powerful chelater of divalent metals (Ho, 2004).

Lead is classified as a probable carcinogen by the "International Agency for Research on Cancer" (IRAC). It promotes mutagenesis when combined with alkilating and oxidizing DNA-damaging agents (McNeill *et al*., 2006). Epidemiologic studies have illustrated a possible, but inconsistent association between occupational exposure to lead and specifically cancers of the kidney, lung and stomach (Lam *et al* 2007). There are only few investigations comparing the plasma levels of trace elements in gastric cancer patient with normal volunteers. Due to higher incidence of gastric carcinoma and the

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probable more exposure of Northern individuals, we conducted this study to address the relevance of Zn and Pb to gastric carcinoma.

MATERIALS AND METHODS

Setting and patients: This study was conducted in Imam Hospital of Sari located in the north of Iran. Thirty two patients with gastric carcinoma diagnosis confirmed by pathological samples and 32 matched healthy volunteers included in the study.

Sampling and analysis: Five milliliter of peripheral blood of patients was added to the vials containing 1 mL of 5% v/v triton-X100 and shacked for 1 h until compete mixing of triton-X100 with blood and lyses of blood cells. Samples were kept at 8°C until the time of analysis. All containers emerged for 24 h in nitric oxide 5%. After calibration, the plasma concentrations of Zn and Pb were measured with flame atomic absorption spectrophotometer.

Statistical analysis: SPSS version 14 software has been used for data analysis. To compare the Pb and Zn levels of patients with control group, student's t-test has been done. p-value<0.05 is considered as significant difference.

RESULTS

The demographic characteristics and the level of Pb and Zn of patients and control group are presented in Table 1. Thirty- two patients were screened for the study and 32 volunteers person were randomized to control group. The average age of patients was 59.63±12.03 years compared with 56.56±11.47 years of control group. 71.9% of patients and 62.5% of control groups were male. That the differences between 2 groups are not significant.

When compared to the results of plasma elements levels between patients and control group; the zn plasma levels in patients and control group were found to be 1.49±0.75 mg L^{-1} and 2.12±0.83 mg L^{-1}, respectively. P.value (0.002) was considered significantly different between the two groups. That Zn plasma level in patients is lower than those in control group.

Table 1: Demographic characteristics and levels of Zn and Pb of patients and control groups

	Groups			
Parameter	Sex (% male/female)	Age (X±SD)	Pb (mg L^{-1})	Zn (mg L^{-1})
Patients (Gastric cancer)	71.9/ 28.1	59.63±12.03	0.76±0.18	1.49±0.75
Control	62.5/37.5	56.56±11.47	0.56±0.07	2.12±0.83
p-value	0.65	0.30	0.00	0.002

The plasma Pb level was found to be 0.76±0.18 mg L^{-1} in patients and 0.56±0.07 mg L^{-1} in control group. According to these results, plasma Pb level in patients is significantly higher than control, (p = 0.000).

DISCUSSION

This study investigated that the Zn content in the plasma of gastric cancer patients was lower than in healthy group and the difference was statistically significant. This finding is similar to some other study (Hua-Dong Lu *et al*., 1999; Sempertegui *et al*., 2007). Zn is one of the necessary compositions of many enzymes in human body, involved in the synthesis of DNA and RNA polymeric enzymes. It took part in the nucleic acid metabolism and immunosurveillance protection, affecting the process of cancer development directly or indirectly (Hua-Dong Lu *et al*., 1999).

There is now increasing evidence that oxidative stress is an important contributing factor in several chronic degenerative diseases, such as cancer (Ho, 2004). Deficiency of essential trace elements (such as Zn) as cofactors of enzymes could severely impair the host's resistance against carcinogenic stress (Yaman *et al*., 2007). For example, chronic H. Pylori infection is the most common cause distal gastric cancer. Other risk factors include dietary nitrite, salt and smoking (Jiangunag and Hemminki, 2006). Overally, many factors have been related to the disease (Barr, 2007). The marked decline in the incidence of gastric cancer in the united state and other industrialized countries suggests that the different environmental exposure play an important role in the pathogenesis of the disease (Fuchs and Mayer, 1995). Other risk factor such as nutritional deficiencies of zinc and environmental exposure to lead and N-nitrosamines play an important role in the pathogenesis of this disease worldwide (Louise *et al*., 2003; Lam *et al*., 2007).

H. Pylori induce oxidative stress while zinc deficiency results in increased sensitivity to it. In addition, the degree of inflammation in H. Pylori-induced gastritis appears to be modulated by gastric tissue zinc concentration (Sempertegui *et al*., 2007). In other study, it has been reported that zinc serum level decreases in patients with atrophic gastritis and gastric adenoma (Magalova *et al*., 1999). In experimental study, Louise *et al*. (2003) showed that dietary zinc deficiency in mice enhances cellular proliferation in esophageal/ forestomach and susceptibility to N-nitrosomethyl benzylamine induced carcinogenesis (Louise *et al*., 2003). Epidemiological studies also indicated that content of Zn in serum of tumor patients was lower than in healthy persons (Lu *et al*., 1999). Similar to our study, other

studies demonstrated that the average zinc concentrations in the cancerous stomach tissue samples were found to be significantly lower than those in the non-cancerous stomach tissue samples (Yaman *et al*., 2007; Sempertegui *et al*., 2007). If zinc plays a critical role in antioxidant defense and maintenance of DNA integrity, it is likely that inadequate zinc will be highly detrimental to these susceptible individuals. Characterization of the mechanisms by which zinc affects DNA integrity will aid in understanding both nutrient-gene and nutrient-environment interactions and will result in a basis for nutrition-based cancer prevention strategies (Ho, 2004).

Lead is the most significant toxin among the heavy metals. Industrial decisions, such as the addition of lead to paints, dyes and gasoline, have created an epidemic of lead poisonings. The association between occupational exposure to lead and specific cancer sites varies among epidemiologic studies. The strongest evidence is for lung and stomach cancer (Lam *et al*., 2007).

In our study, we compared plasma Pb levels of gastric cancer patients with. We found that the Pb level of healthy persons was significantly higher than the volunteer persons. Other studies suggest an association between occupational exposure to inorganic lead and cancers (Carta *et al*., 2005; McNeill *et al*., 2006). Lam *et al*. (2007) reviewed the studies which discussed the association between stomach cancer and lead exposure. Three studies found elevations for stomach cancer in lead-exposed workers, while 2 others did not (Lam *et al*., 2007). Lead inhibits the in vitro repair activity of AP1, the major endonuclease for repairing mutagenic and cytotoxic abasic sites in DNA (McNeill *et al*., 2006). It has been reported that higher Pb level could lead to other diseases such as cardiovascular diseases. Blood lead levels as low as 5-9 μg dL^{-1} was associated with an increased risk for death from all causes (Schober *et al*., 2006).

Such as other clinical studies, there are some limitations for our study. Cancer development is really a complex phenomenon which several risk factors may affect it. Family history, exposure to carcinogens and the diet of individuals are some examples that have not been considered in our study.

CONCLUSION

In conclusion, gastric cancer patients had a lower Zn level and a higher Pb level compared to healthy volunteers. This study emphasizes the critical role of trace elements as a risk factor for development of cancer. The consistency of our results with other studies would confirm the potential benefit of using the favorable trace elements (e.g., Zn) and also the chelators of heavy metals (e.g., Pb) for prevention of gastric cancer in high risk individual..

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