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Original research article

The association between blood cadmium levels and the risk of gastrointestinal cancer in Tabriz, northwest of Iran

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ABSTRACT

Introduction: Cancer is a major health problem worldwide. Gastrointestinal tract malignancy is one of the most common forms of cancer around the world. Occupational exposure to the heavy metals including cadmium was defined as one of the most important environmental risk factors involved in initiation of cancer. Cadmium, a toxic and non-essential heavy metal, was classified as group 1 carcinogen.
Aim: The aim of this study was to investigate the association between blood cadmium levels and the risk of gastrointestinal cancer in cancer patients.
Material and methods: This descriptive study was carried out on 111 gastrointestinal cancer patients as cases and 111 healthy people as controls from January to October 2013 in Tabriz, northwest of Iran. The protocol of this study is approved by the Ethics Committee in Tabriz University of Medical Science. Considering inclusion criteria, participants were selected randomly and a written informed consent was filled out for each patient. Demographic data were obtained by questionnaire. Blood samples (5 mL) were collected from each patient in fasting status and analyzed by graphite furnace atomic absorption spectrophotometer (GFAAS).
Results and discussion: Blood cadmium levels were significantly higher in cancer patients compared to healthy individuals ($P = 0.037$). The results of multivariate regression model did not show significant association between the concentrations of blood cadmium and the risk of gastrointestinal cancer: $P = 0.137$, OR = 1.15 (95% CI; 0.96–1.38).
Conclusion: Our data suggest that finding individuals with high blood cadmium level and then lowering this amount can be considered as important strategy to prevent gastrointestinal cancer.

1. Introduction

Nowadays, the main reason for human morbidity and mortality have been changed from infectious to non-communicable diseases.[1] Cancer, uncontrolled growth and spread of abnormal cells, has been known as one of the leading causes of death in both developed and developing countries.[2,3] About 14.0 million new cases of cancer and 8.2 million deaths were occurred worldwide in 2012.[4] Among all kinds of malignancies, gastrointestinal tract (GI) cancer is one of the most common malignancies in both genders worldwide.[5] GI cancer is responsible for 20% of estimated new cancer cases and 15% of estimated deaths in the world.[6]

Cancer incidence is due to both genetic and environmental factors.[2] It was suggested that environmental factors accounts for 80% of cancer causes.[7] The most serious environmental risk factors which involved in carcinogenesis, are unhealthy lifestyle habits like smoking, consumption of alcohol, physical inactivity, unhealthy dietary habits and occupational factors.[6] Recently, it was shown that some trace elements have main roles in carcinogenesis. These chemical elements present in minute quantities and find naturally in environment.[8] Trace elements such as arsenic (As), cadmium (Cd), nickel (Ni), selenium (Se), and zinc (Zn), are

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associated with human health by various routes.[8] Many studies confirmed that cadmium could involve in most malignancies in the body. Cadmium, a toxic and non-essential heavy metal with half-life 10–30 years, has been classified as group 1 carcinogen. Carcinogenicity of cadmium in many organs such as kidney, lung, breast, liver, prostate, bladder and pancreas was manifested in many animals and human studies.[6] It was shown that cadmium develops cancer via genotoxic effects,[9] inhibition of apoptosis, DNA repair[9–11] and activation proto-oncogenes.[12,13] Human exposure to cadmium occurs through air pollution and contaminated water and food.[14] One of the most important risk factors for cancer development is the accumulation of cadmium in circulation.[15] After exposure, blood level of cadmium increases rapidly until it reaches a concentration that manifested the intensity of exposure.[16] However, when cadmium exposure stops, its levels in the blood never return to the pre-exposure concentration.[15]

We proposed that gastrointestinal cancer patients have higher levels of blood cadmium in comparison to healthy individuals. Considering the lack of study in this field in Iran, the present study was conducted to investigate blood cadmium levels in gastrointestinal cancer patients in Tabriz, Iran.

2. Aim

The aim of this study was to investigate the association between blood cadmium levels and the risk of gastrointestinal cancer in cancer patients.

3. Material and methods

This comparative study was carried out from January to October 2013 in Tabriz, northwest of Iran. The sample size was calculated by using G-Power software, setting α-error probability at 0.05, power (1-β-error probability) at 0.95% according to the similar study.[17] Finally, 111 gastrointestinal (esophagus, gastric, colon, rectum) cancer patients as a case group and 111 healthy people as a control group were allocated.

All participants were recruited from Imam Reza Hospital, the largest hospital in northwest of Iran. The protocol of this study was approved in the Ethics Committee in Tabriz University of Medical Sciences (No 5/4/2787). The patients for this study were aged between 30 and 70 with confirmed GI cancer.

Individuals with kidney diseases, anemia, pregnant women, historical gastric surgery and consumption of zinc, iron, calcium and selenium supplements were not included in the study.

After explanation the nature of the study, participants completed a written consent form. Demographic data including age, gender, type of cancer, smoking and anthropometric measurements were collected by questionnaire. Weight was measured using a Seca scale (Seca, Hamburg, Germany) in kilograms with precision of 0.1 kg with light clothes. Height was measured using a stationmaster (Seca) in meters with precision of 1.0 mm without shoes and BMI was calculated, as weight (in kilograms) divided by the square of height (in meters). Blood samples (5 mL) were collected after 12 h fasting state and frozen in −70 °C until analysis.

We applied dry ashing digestion method to prepare samples for measuring cadmium. Samples were ashed in electric furnace at 550 °C (Excition, Tehran, Iran) and then residues digested in HCl.[18] A Varian 240 AAFF graphite furnace atomic absorption spectrophotometer (GFAAS) was used for measuring of blood cadmium concentration. Cadmium was measured in 228.8 nm wavelength. The GFAAS standard curve was obtained by standard soluble (5 μg/L, 15 μg/L and 30 μg/L) and the concentration of cadmium was adjusted for bloodcreatinine level.

3.1. Statistical analysis

The data were analyzed by SPSS software (v. 16:0, Shikagho, IL, USA). Quantitative data were reported as mean ± standard deviation (SD) and qualitative data presented as frequency (percentage). Normality of data was assessed using Kolmogorov–Smirnov test. Independent-sample *t*-test was applied to compare difference between the study groups. Analysis of variance (ANOVA) test was used for comparison of differences in blood cadmium and type of cancer. Chi-square test was used to examine differences in qualitative variables in both groups. Univariate and multiple regression models were conducted to determine odds ratio (OR) of blood cadmium risk and GI cancer. Confounding factors defined as age, gender and smoking status. Statistical significance was considered as $P < 0.05$.

4. Results

Mean ages of participants were 58.67 ± 9.93 years in cancer patients and 52.03 ± 12.16 in healthy individuals ($P < 0.001$). In total, 55% of patients were males; however, about 40% of healthy people were males. About 27% of cases and 18% and controls patients were smoking cigarettes. There were no significant difference in the smoking status ($P > 0.05$). About 36.9% of patients had stomach cancer and 11.7% of them had esophagus cancer. Demographic characteristics of participants are shown in Table 1.

The results showed that blood cadmium levels in cancer patients were significantly higher than in healthy individuals ($P = 0.037$). Table 2 depicts the concentration of blood cadmium in both case and control groups, separately.

Blood cadmium concentration in females was higher than in males with exception on gastric cancer, however, there was no significant differences between two groups ($P > 0.05$). The mean concentration of blood cadmium in smokers was higher than in non-smokers; however this difference was not significant (2.67 ± 1.84 vs 2.25 ± 1.62, respectively). Fig. 1 depicts the blood cadmium differences in both genders.

Based on the results of simple logistic regression (unadjusted OR's), blood cadmium concentration, sex and age were significantly related to cancer incidence ($P < 0.05$); males had the odds of cancer incidence 76% more than females. With an increase in age and blood cadmium concentration in one year and 1 μg/L the odds of cancer incidence increased 5% and 18%, respectively.

Considering that smoking is one of the major sources of cadmium, this factor entered to simple logistic regression and the results showed that smokers had the odds of cancer incidence 67%

Table 1
Demographic characteristics of participants ($n = 222$).

Variables	Cases ($n = 111$)	Controls ($n = 111$)	*P*
Age, year	58.67 ± 9.93	52.03 ± 12.16	**0.001***
Gender, *n* (%)			
Male	61 (55.0)	45 (40.9)	**0.044****
Female	51 (45.0)	65 (59.1)	
Type of cancer, *n* (%)			
Esophagus	13 (11.7)		
Stomach	41 (36.9)	–	
Colon	39 (35.2)		
Rectum	18 (16.2)		
Smoking statue, *n* (%)			
Yes	30 (27.0)	21 (18.2)	0.116**
No	81 (73.0)	90 (81.8)	
Weight, kg	66.42 ± 9.2	69.80 ± 8.8	0.054*
BMI, kg/m^2	25.18 ± 2.7	25.69 ± 3.3	0.190*

*Independent Student's *t*-test; **χ^2 test; bold indicates significant results ($P < 0.05$).

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