Serum Strontium and Antimony Levels in Patients with Esophageal Cancer and Healthy People

Shima Akbari Rad (MSc)
Department of Clinical Biochemistry, Faculty of Medicine, Golestan University of Medical Sciences, Gorgan, Iran

Hamid Reza Joshaghani (PhD)
Department of Clinical Biochemistry, Gastroenterology and Hepatology Research Center, Golestan University of Medical Sciences, Gorgan, Iran

Masoud Khoshnia (MD)
Department of Internal Medicine, Gastroenterology and Hepatology Research Center, Golestan University of Medical Sciences, Gorgan, Iran

S.Mehran Hosseini (MD, PhD)
Department of Medical Physiology, Faculty of Medicine, Golestan University of Medical Sciences, Gorgan, Iran

Corresponding author:
S.Mehran Hosseini

Email: hosseini@goums.ac.ir

Tel: +989368761586

Address: Faculty of Medicine, Golestan University of Medical Sciences, Gorgan, Iran

Received : 03 Feb 2015
Revised: 05 Sep 2015
Accepted: 29 Sep 2015

ABSTRACT

Background and Objective: Esophageal cancer is the third most common type of cancer in Iran. In Golestan province of Iran the environmental concentration of antimony and strontium in areas with high prevalence of esophageal cancer is higher.

The carcinogenic effects of strontium have been reported, but carcinogenicity of antimony is still unclear. Since there is not enough information regarding the relationship between the concentration of strontium and antimony and prevalence of esophageal cancer in the province, this study aimed to evaluate serum levels of these elements in patients with esophageal cancer using atomic absorption spectroscopy.

Methods: This study was performed on 30 patients with esophageal squamous cell carcinoma and 30 healthy matched controls. After sampling, The serum concentrations of strontium and antimony were measured using atomic absorption spectroscopy.

Results: Half of the esophageal cancer patients and control participants were male. The mean age of patients and controls was 66 $\pm$ 13 and 64 $\pm$ 8 years, respectively. The mean serum concentration of strontium in patients and controls was 24.18 $\pm$ 1.62 and 24.08 $\pm$ 1.46 µg/L, respectively. The mean serum concentration of antimony in patients and controls was 18.61 $\pm$ 1.48 and 18.98 $\pm$ 1.93 µg/L, respectively. No statistically significant difference was observed between the serum concentrations of the two elements in patients and controls.

Conclusion: There is no difference between serum levels of strontium and antimony in cancer patients and healthy controls, which could be due to tissue accumulation.

Keywords: Antimony, Strontium, Esophageal Neoplasms.

This paper should be cited as: Akbari Rad SH, Joshaghani HR, Khoshnia M, Hosseini SM[Serum Strontium and Antimony Levels in Patients with Esophageal Cancer and Healthy People]. mljgoums. 2016; 10(4): 9-13

INTRODUCTION

In Iran, esophageal cancer is the second most common type of cancer (after gastric cancer) in men and the third most common type of cancer in women. It is estimated that nearly 5,800 Iranians die because of esophageal cancer each year. The incidence rate of esophageal cancer in Northeast of Golestan Province was reported as 100 per 100,000 men and women, 35 years ago (1).

Antimony (Z=51) is an element with molecular weight of 121.76 g/mol that can be found in mines. Antimony is not abundant in nature and its carcinogenic effects have not yet been determined. There is a limited amount of information about the toxic effects of antimony on nature and human's health. Most of the available information about antimony is resulted from studies on organic compounds with medicinal applications. Moreover, there is no accurate data regarding the internal absorption of antimony in humans (2). Strontium is a non-essential metal that cannot be found free in nature and often produces strontium oxide. It ranks about 15th among the elements found in the earth that makes up approximately 0.02–0.03% of the earth's crust. This element can be found in water, soil, air and living organisms. It is among environmental (agricultural, industrial, transportation) pollutants that can enter human body via the soil-plant-food cycle. The most important applications of strontium are in glass-making factories and processing of zinc (3). Study of Keshavarzi et al. (2012) in the Golestan Province evaluated the amounts of strontium and antimony in drinking water of 45 villages with high incidence of esophageal cancer.the measured values in the mentioned study were higher than the maximum allowed limits set by the World Health Organization. Moreover, there was an association between high levels of these elements and prevalence of esophageal cancer in this province (4). The same researchers also conducted a study on agricultural soil and grain samples in the Golestan Province in 2012. The villages were divided into two groups based on the prevalence of esophageal cancer. The results showed the association of high levels of antimony and strontium with risk of developing esophageal cancer in areas with high incidence rate (5).

To our knowledge, there is no study regarding the association of strontium and antimony concentrations and esophageal cancer in areas with high prevalence of esophageal cancer such as the Golestan Province. Therefore, this study aimed to measure these trace elements in patients with esophageal cancer using atomic absorption spectroscopy.

MATERIAL AND METHODS

In this cross-sectional study, 30 patients (15 females and 15 males) with esophageal squamous cell carcinoma and 30 healthy individuals (15 females and 15 males) were enrolled. The serum concentrations of strontium and antimony were measured using an atomic absorption spectrometer. For the measurement of antimony, serum was diluted with diluent containing 1.0556 μl ascorbic acid, 50 μl Triton x100, 50 μl anti-foam and 12.5 μl distilled water. Then, the mixture was injected to the device by adding a modifier solution containing 10 mg palladium chloride, 100 μl hydrochloric acid and 10 ml distilled water. Strontium was diluted with 1% nitric acid and then injected to the device along with palladium chloride modifier solution. Standard curve was plotted using 5, 10, 20, 30 and 40 μg/L concentrations of strontium and antimony standards. After entering the data into SPSS software (version 16), data were described using mean and standard deviation (SD). Kolmogorov-Smirnov test was used to evaluate the normality of data distribution. Independent T-test was used to compare serum levels of the elements between the two groups. P-values less than 0.05 were considered as statistically significant.

Commercial standard solutions of strontium and antimony were produced by specific temperature programs (Table 1 and 2).

RESULTS

The mean age of patients and healthy controls was 66.86 ± 13.08 and 64.13± 8.32 years, respectively (Table 3).

The serum strontium and antimony levels in patients and controls showed no significant difference. In addition, the serum concentrations of the two elements in both groups were not significantly different in terms of age, gender and body mass index.

Table1- Strontium temperature program

Id	Step	Start Temperature (^oC)	End Temperature (^oC)	Time (sec)	Inner Gas	Mode
1	Dry1	50	120	50	On	Power
2	Dry2	120	140	20	On	Power
3	Ash1	140	400	15	On	Power
4	Ash2	400	400	10	On	Power
5	Ash3	400	400	3	Off	Power
6	Atom	2700	2700	3	Off	Power
7	Clean	2800	2800	3	On	Power
8	Cooling	0	0	30	On	Power

Table 2-Antimony temperature program

Id	Step	Start Temperature (^oC)	End Temperature (^oC)	Time (sec.)	Inner Gas	Mode
1	Dry1	5	70	45	On	Power
2	Dry2	70	120	10	On	Power
3	Dry3	120	140	15	On	Power
4	Ash1	140	400	30	On	Power
5	Ash2	400	1000	10	On	Power
6	Ash3	1000	1000	5	On	Power
7	Ash4	1000	1000	4	Off	Power
8	Atom	2400	2400	3	Off	Power
9	Clean	2700	2700	3	On	Power
10	Cooling	0	0	30	On	Power

Table 3- Demographic characteristics of patients and controls (mean ± SD, n = 30)

Body mass index (kg/m^2)	Height (m)	Weight (Kg)	Gender (%)		Age (years)	Variable
			Female	Male		Group
23.19±1.85	1.65±8.26	64.93±7.65	%50	%50	64.13±8.32	Control
22.79±2.98	1.65±8.93	62.33±1.05	%50	%50	66.86±1.30	Patient

Table 4- Comparison of mean ± SD serum strontium (Sr) and antimony (Sb) levels in the two study groups

P-value	Concentration (µg/L)	Group	Element
0.805	24.08±1.46	Control	Strontium
	24.18±1.62	Patient	
0.410	18.98±1.93	Control	Antimony
	18.61±1.48	Patient	

DISCUSSION

In this study, the levels of strontium and antimony in cancer patients and healthy controls showed no statistically significant difference. This is inconsistent with the results of Pasha and Cihan that showed higher concentrations of strontium and antimony in cancer patients compared to healthy controls (6,7). These elements are present in organic and inorganic forms in foods and drinking water respectively. Their absorption in the small intestine is low. The exposure time of large intestine mucosa to these elements may be important.

Since most elements are absorbed from food and not from drinking water there is not sufficient evidence to discuss the relationship between these trace elements-related disease and drinking water (8). For this reason, the results of the present study require further investigations to determine the association of concentrations of trace elements in drinking water and food with esophageal cancer. Due to rapid urinary excretion of antimony, it is appropriate to measure its levels in urine. There seems to be a correlation between exposure to antimony and its urinary excretion. Some studies have reported the amount of antimony in respiratory samples (9). Studies show that the lack of distinct genotoxic effects of antimony may be due to minor exposure to this element. Although *in vivo* and *in vitro* studies have shown the genotoxic effects of antimony, the amount of exposure to the element in those studies were higher than the amounts measured in the present study. Damage to the DNA and its repair mechanisms has been suggested as the possible carcinogenic effect of antimony and its compounds (10). It is difficult to determine increases in antimony levels because of the low amounts of this element in the body. In study of Gebel et al. the majority of control individuals had quantities below the analytical detection limit for this element. In this study, 89 out of 196 people in an area and 57 out of 75 people in another area had less than 0.5 μg/L concentrations of antimony (11). Lack of significant difference between the two groups with limited sample size in the mentioned study could be due to the low level of this element. Studies of Kikuchi et al. and Nakaji et al. have shown indirect evidence of the carcinogenic properties of strontium. Kikuchi et al. showed a correlation between the amounts of strontium in drinking water of a region in Japan and prevalence of colon cancer in women of that region. Another study on the same group of subjects showed a significant relationship between stomach cancer mortality rates among men and women and concentrations of strontium in drinking water (8, 12). The amount of strontium received daily through diet is different depending on the geographic location and type of foods consumed by the person. Moreover, significant differences have been reported for the amounts of this element in each individual. This element is mainly excreted by the kidneys, which increases the risk of its accumulation in patients with renal disease (13). This could justify the difference between the results of the present study and other studies, because gastrointestinal disorders, renal disease and the type of diet could affect the amount of this element. Since strontium mainly accumulates in bones, it is either excreted or used in growing bones in case of bone resorption. Variation in the process of its excretion can also affect the amount of strontium in the blood (14). Strontium is excreted in the sweat, feces and mainly by urine. Although the exact mechanism of strontium excretion has not been determined the specific gravity and creatinine are the two factors that are used to modulate the excretion of this element (15).. Consideration of these factors can improve the comparison, analysis and interpretation of the results.

CONCLUSION

Overall, the study shows no significant correlation between serum levels of strontium and antimony in patients with esophageal cancer. Therefore, more studies with new designs and larger number of participants are required to determine the possible association of these two elements with esophageal cancer.

ACKNOWLEDGMENTS

The authors would like to express their gratitude to the Deputy of Research and Technology of Golestan University of Medical Sciences for approval of this study (No. 930 918 174) and financial support. The cooperation of all participants is gratefully acknowledged.

CONFLICT OF INTEREST

We have no conflict of interest to declare.

REFERENCES

1. Malekzadeh R, Semnani S, Sadjadi A. *Esophageal Cancer in Iran A Review.* Middle East Journal of Cancer. 2010; 1(1): 5-14.

2. Smichowski P. *Antimony in the environment as a global pollutant: a review on analytical methodologies for its determination in atmospheric aerosols* .Talanta. 2008; 75(1): 2-14. doi: 10.1016/j.talanta.2007.11.005.

3. Pors Nielsen S. *The biological role of strontium.* Bone. 2004; 35(3): 583-8.

4. Keshavarzi B, Moore F, Najmeddin A, Rahmani F, Malekzadeh A. *Quality of drinking water and high incidence rate of esophageal cancer in Golestan province of Iran: a probable link.* Environmental geochemistry and health. 2012; 34(1): 15-26.

5. Keshavarzi B, Moore F, Najmeddin A, Rahmani F. *The role of selenium and selected trace elements in the etiology of esophageal cancer in high risk Golestan province of Iran.* Science of the Total Environment. 2012; 433: 89-97. doi: 10.1016/j.scitotenv.2012.04.033.

6. Pasha Q, Malik SA, Shah MH. *Statistical analysis of trace metals in the plasma of cancer patients versus controls.* Journal of hazardous materials. 2008; 153(3):1215-21.

7. Cihan YB, Sözen S, Yıldırım SÖ. *Trace elements and heavy metals in hair of stage III breast cancer patients.* Biological trace element research. 2011; 144(1-3): 360-79. doi: 10.1007/s12011-011-9104-z.

8. Kikuchi H, Iwane S, Munakata A, Tamura K, Nakaji S, Sugawara K. *Trace element levels in drinking water and the incidence of colorectal cancer.* The Tohoku journal of experimental medicine. 1999; 188(3): 217-25.

9. Lüdersdorf R, Fuchs A, Mayer P, Skulsuksai G, Schäcke G. *Biological assessment of exposure to antimony and lead in the glass-producing industry.* International archives of occupational and environmental health. 1987; 59(5): 469-74.

10. Cavallo D, Iavicoli I, Setini A, Marinaccio A, Perniconi B, Carelli G, et al. *Genotoxic risk and oxidative DNA damage in workers exposed to antimony trioxide.* Environmental and molecular mutagenesis. 2002; 40(3): 184-9.

11. Gebel TW, Suchenwirth R, Bolten C, Dunkelberg HH. *Human biomonitoring of arsenic and antimony in case of an elevated geogenic exposure.* Environmental health perspectives. 1998; 106(1): 33-9.

12. Nakaji S, Fukuda S, Sakamoto J, Sugawara K, Shimoyama T, Umeda T, et al. *Relationship between mineral and trace element concentrations in drinking water and gastric cancer mortality in Japan.* Nutrition and cancer. 2001; 40(2): 99-102.

13. Schrooten I, Elseviers MM, Lamberts LV, De Broe ME, D'Haese PC. *Increased serum strontium levels in dialysis patients: an epidemiological survey.* Kidney international. 1999; 56(5): 1886-92.

14. Cohen-Solal M. *Strontium overload and toxicity: impact on renal osteodystrophy.* Nephrology Dialysis Transplantation. 2002; 17(suppl 2): 30-4.

15. Usuda K, Kono K, Hayashi S, Kawasaki T, Mitsui G, Shibutani T, et al. *Determination of reference concentrations of strontium in urine by inductively coupled plasma atomic emission spectrometry.* Environmental health and preventive medicine. 2006; 11(1): 11-6.