Original Article

SILICA AND ESOPHAGEAL CANCER IN GOLESTAN PROVINCE NORTHEAST OF IRAN

Sima Besharat[1], Ali Jabbari[2], Shahryar Semnani[3]

ABSTRACT

Objectives: Association of silica with diseases like cancers has been determined previously. This study was designed to determine the quantity of silis in flour produced in Golestan province and its relation to the esophageal cancer.

Methodology: We took flour samples from all flour mills in Golestan province. Base-melting method in nickel cruise was used in 550°c; the extract was reduced with acid. The differences between silis concentration in various regions were compared. P-value <0.05 was assumed significant.

Results: Median silis concentration was 0.0030grams, mean was 0.008760 ± 0.004265 (SD) grams in each 100 grams flour. The differences in mean silis concentrations of various regions were not significant (P>0.05).

Conclusions: This study did not show high level of silica in the flour of Golestan province. We could not find significant differences between silica contaminations in the various areas. Further studies on the consumed bread and rice in the various regions of the province can be helpful.

KEYWORDS: Silis, Flour, Contamination, Esophageal cancer.

Pak J Med Sci October - December 2007 (Part-II) Vol. 23 No. 6 898-902

INTRODUCTION

Silica (SiO2) is an oxide of silicon. It is an abundant mineral in rock, sand, and soil. Its existence in food products is a presentation of contamination.[1] Silica dust is an inhalation hazard. Some occupations have a high potential for exposure to crystalline silica dust and consequent silicosis. It has been estimated that more than two million workers are exposed to silica dust in the general maritime and construction industries. Silica is used in pharmaceutical industries, too.[2]

On one hand, in several studies, association of silica with diseases like cancers has been evaluated.[1] But on the other hand, some biological functions of Silica are known. Silicon has been discovered to be an important trace element necessary for cartilage and bone tissue formation. Silicates are essentially non-toxic when taken orally as antiacid (magnesium trisilicate).[3]

Biological reactions of Silica are due to the stimulation of the Immune System. Both Innate and Adaptive Immunity are involved. Silicosis can be considered as a "Collagen" Disease, related to other diseases like Rheumatoid Arthritis, Lupus erythematosus and Scleroderma. Some people have suggested that the relation-

1. Dr. Sima Besharat,
Research Scientist,
2. Dr. Ali Jabbari,
Research Scientist,
1,2: Golestan Research Center of
Gastroenterology and Hepatology,
Golestan University of Medical Sciences, Iran.
3. Dr. Shahryar Semnani,
Associated Professor of Golestan University,
Gastroenterologist, Dept. of Gastroenterology,
Golestan Research Center of
Gastroenterology and Hepatology (GRCGH), Iran.

Correspondence

Dr. Ali Jabbari,
No 36, Farhangian Township,
Gorgan City, Golestan Province,
Postal code: 49148-15855, Iran.
E-mail: dr_besharat_jabbari@yahoo.com

* Received for Publication: June 4, 2007
* Revision Received: September 25, 2007
* Revision Accepted: September 26, 2007

ship between Silica and immune system can work as a two-headed sword.[3]

Not surprisingly; the incidence of these diseases has been shown to be significantly increased in human exposed to Silica. Some nutritional investigators speculate that a silica mineral deficiency is involved in the causation of several human disorders including atherosclerosis, osteoarthritis, and hypertension, as well as, the aging process.[3]

The excess risk of esophageal cancer mortality among caisson workers with silicosis could be explained best by the very heavy exposure to free silica dust in their working environment. An increased mortality risk of esophageal cancer (EC) among silicotics who had worked in underground caissons after adjusting for cigarette smoking and alcohol drinking was seen.[4-7] Ingestion of silica particles after lung clearance may increase the risk of EC among workers exposed to silica.[7]

The International Agency for Research on Cancer (IARC) classified crystalline silica as a known human carcinogen. Exposure to crystalline silica has been associated with an increased risk of developing lung cancer. Previous studies have also documented an association between airborne silica exposure and other health problems, including chronic obstructive pulmonary disease, rheumatoid arthritis, scleroderma, Sjogern's syndrome, lupus, and renal disease,[2] but the relationship between silica and EC must be evaluated further.

The northeastern part of Iran in Golestan province is known to have the highest incidence of esophageal cancer in the country and one of the highest areas in the world.[8] Examination of the seeds of wheat in this region showed that the fiber originates from the seeds of the common Mediterranean grass Phalaris minor can contaminate the wheat. The investigators presented a hypothesis for the involvement of these plant mineral fibers (contain high concentration of silica) in the etiology of esophageal cancer in Iran and in other areas of high incidence.[9]

This study was designed to determine the relationship between silica, as a known human carcinogen, and esophageal cancer, in Golestan province, northeast of Iran, which is known as a high incidence area of esophageal cancer in the world.

METHODOLOGY

This descriptive study was started in spring 2005 and lasted about 18 months, with the support of "Food and Drug Committee" of Golestan University of Medical Sciences. Bread is the main food in this area and flour contamination was considered as the indicator of silica contamination. Flour samples were collected from all flour manufactures in Golestan province.

We categorized Golestan province into three parts, according to the incidence and prevalence of esophageal cancer and from geographical point of view then we located the mill manufactures in this area due to our classification. Census method was used to get the samples. Three samples were collected from each factory, at different times. Samples were transported to the specific chemical laboratory, under the tight controlled condition. We choosed an equal weight of the samples of each manufacture and mixed them, this blended sample was considered as the final sample of each factory (250 grams).Base-melting method in nickel cruise in 550°c was used for burning and the extract was reduced with acid. The complex was evaluated with spectrophotometer (820 nanometer wavelength). Extraction method is a less known method in food products, therefore five control samples of wheat seeds and five control samples of wheat pedicles were examined. The concentrations of silis that were measured in control samples were equivalent with the standard tables.[10] Recommended Dietary Allowance / Intake (RDA / RDI) of this material are not mentioned. Table-I

All the chemical procedures were rechecked. Then data were matched with the location of manufacturers based on our categorization. We pointed the location of the manufactures and the result of the chemical analysis of flour on the map of Golestan province. Data was

Table-I: Standard values of silica suggested in International measurements

Certain groups	*Suggested dose*
More 18 years old	5mg - 20mg
estimated daily	20mg - 50mg
intake of silicon	
Therapeutic Range	10mg - 300mg
In the form of horsetail	500mg - 6,000mg

entered into SPSS-12, central, distributive indices were calculated and the differences between silis concentration in various regions were compared with non-parametric Kruskul Walis test. P-value < 0.05 was assumed significant. Results were discussed with specialists.

RESULTS

Generally, median silis concentration was 0.0030 grams, mean concentration was 0.008760 ± 0.004265 (standard deviation), minimum was 0.003 and maximum was 0.018 grams in each 100 grams flour produced in province's factories. Statistical analyses regarding the mean concentration differences were not done between different areas, because of the small sample size; median was compared with nonparametric test.

As shown in Table-II, mean silis concentrations were 0.012, 0.01 and 0.003 in Gorgan and the central part of the province, western and eastern part, respectively. The differences were not statisticaly significant [Ï÷2 = 3.259, P=0.196] (Table-II). The differences between silis median concentrations in wheat seeds, pedicles and flour were statistically significant (P-value<0.05). (Table-III)

Table-II: Median concentration of silis (gr/100 grams) regarding to the area of Golestan province

Median concentration of Silica	*Area*
0.003	East
0.010	West
0.012	Center

Table-III: Silica concentration in seed, pedicle of the wheat (control) and flour in Golestan province

Median silica concentration (gram in 100 grams)	
1.88	pedicle of the wheat
0.0166	seed of the wheat
0.00876	Wheat flour

DISCUSSION

Some studies have revealed to the probable role of silica exposure and diseases like esophageal cancer, but its definite effect has not been confirmed, yet. The results of a case-control study of the relationships among silica exposure, gastric cancer, and esophageal cancer in Japan, suggested that gastric and esophageal cancer were related to silica exposure and silicosis in that study area, although they did not reach a statistically significant level because of the small sample size. The estimated odds ratios were higher for esophageal cancer and silicotic patients.[11]

O'Neill et al reported the high contamination with fibrous silica contaminant in the diet of north-east of Iran where esophageal cancer has a very high incidence (Turkman Sahra).[9] In the present study we found out that the total amount of silis in the flour is in the normal range in this area. May be the modern and new purification technologies have been effective in this results. In O'Neill report, low quality of wheat and its contamination to weed and sand was considered important.[9] At the present time the flour contamination to ash and its humidity are measured intermittently by different methods and under the supervision of special organizations. Thus the previous contaminants can be supposed less important. We measured the total amount of silis in the flour with regard to a fine point that a great deal of silis is omitted from the flour during the preparing process.

Our findings suggest that there are not significant differences between the various area flours, revealed less important role of silis in the esophageal cancer but from the medical

point of view it is important. Despite the differences between the present results and previous studies, we can not rule out the probable role of this element in the etiology of the esophageal cancer.

In 1986 Newman found out that certain plants contain structures consisting of biogenic silica. This form of silica has been supposed to be causative agent in the high cancer areas of Southern Africa, Northeast Iran and North of China.[1]

O'Neill et al reported an association of silica fibers in the millet bran and esophageal tumors in another study.[11] Millet bran is a component of the diet in the area of highest esophageal cancer incidence in northern China. Millet bran was found to contain up to 20% by weight of silica; some of this silica occurs as friable sheets or sharply-pointed fibers. These types of silica in millet bran are the most likely source of an unusual contamination with fragments of silica found in the esophageal mucosa surrounding tumors in patients in northern China. If such fragments enter the mucosa, they must cause some degree of trauma, and they may also be able to stimulate proliferation by providing anchorage. These findings suggest the possibility that silica particles might be involved in the etiology of esophageal cancer.[11] The International Agency for Research on Cancer (IARC) suggested silica as a known carcinogen,[10] so in this study silis was considered as a carcinogen, not its compound or its biologic derivatives. So the total silis concentration was noted and the electronic microscope was not assumed necessary to measure the fibers in the flour, which has been used in O'Neill's studies.[9]

Calvert et al in 2003 reported an association between exposure to crystaline Silica and some disease like lung cancer, COPD and pulmonary tuberclosis. They also supported the association between silica exposure and Rheumatoid arthritis, but they did not mention about esophageal or gastric cancer.[12]

Some other investigations revealed this important fact that exposure to the silica dust can be a predisposing factor to the esophageal cancer in workers of caissons and other industries exposed to the silica crystalline.[4-7,13-14] Perhaps, the oral or inhalation absorption of silis has an effect on its carcinogenicity.

A case-control study of lung cancer was done among sugar cane farmers in India 1999, that supported this opinion. Exposure to fibers of biogenic amorphous silica may increase risk of lung cancer among sugar cane farmers.[15] We estimate that it would not play a role as the predisposing factor when we eat it.

A historical cohort study showed an increased mortality risk of esophageal cancer among silicotics who had worked in underground caissons in Hong Kong after adjusting for cigarette smoking and alcohol drinking. Authors believed that the excess risk of esophageal cancer mortality among caisson workers with silicosis could be best explained by the very heavy exposure to free silica dust in their working environment.[4] In that study, the contact method to silica dust was not considered as a confounding factor.

Pan et al reported a relationship between occupational exposure to silica dust and the risk of Esophageal Cancer (EC). They supposed that the ingestion of silica particles after lung clearance may increase the risk of Esophageal Cancer (EC) among workers exposed to silica.[3] Magnesium trisilicate is widely used as an anti acid, but there is not any report about increasing in Esophageal Cancer (EC) in customers and it proved so. It is said that silicates are essentially non carcinogen when taken orally as antacids.[3]

As discussed above, different results are available about the significant relationship between silis exposure and Esophageal Cancer (EC), some are in agreement and suggest etiological role for silis or propose silis as predisposing factor, and others are in disagreement. The distribution of esophageal cancer in Golestan province is not concordant with the silis amounts reported in this study. Silica concentration was higher in the west part but esophageal cancer is higher in the east. Despite the high incidence of esophageal cancer in Northeast of Iran, no significant differences

were seen between silis in wheat flour of this area and the standard measures.

We could not confirm the hypothesis of high contamination of the flour in this area, which was considered important risk in increasing esophageal cancer in the Golestan province that was assumed in previous studies. As such complementary studies are needed to examine the role of environmental factors in the occurrence of gastrointestinal cancers in the area. Studies on the consumed breads and rice in the various regions of the province are needed which can be more helpful.

ACKNOWLEDGEMENTS

Authors wish to thank "Food and Drug Committee" of Golestan province that helped us in data collection, especially Dr. Hamidreza Yazdi MD, Dr. Abbas-ali Keshtkar MD, PhD and Naser Behnampour MSc for their statistical supports and Mr. Naderi for his cooperation in chemical analysis.

REFERENCES

1. Newman R. Association of biogenic silica with disease. Nutr Cancer 1986;8(3):217-21.
2. Yassin A, Yebesi F, Tingle R. Occupational Exposure to Crystalline Silica Dust in the United States, 1988–2003. Environ Health Perspect 2005;113(3):255-60.
3. Pernis B. Silica and the immune system. Act Biomed Ateneo Parmense 2005;76 Suppl 2:38-44.
4. Yu IT, Tse LA, Wong TW, Leung CC, Tam CM, Chan AC. Further evidence for a link between silica dust and esophageal cancer. Int J Cancer 2005;10:114(3):479-83.
5. Tsuda T, Mino Y, Babazono A, Shigemi J, Otsu T, Yamamoto E. A case-control study of the relationships among silica exposure, gastric cancer, and esophageal cancer. Am J Ind Med 2001;39(1):52-7.
6. Siemiatycki J, Germ M, Dewar R, Lakhani R, Begin D,Richardson L. Silica and cancer associations from a multicenter occupational case-referent study. IARC Sci. Publ. 1990;97:129-42.
7. Pan G, Takahashi K, Feng Y, Liu L, Liu T, Zhang S, et al. Nested case-control study of esophageal cancer in relation to occupational exposure to silica and other dusts. Am J Ind Med 1999;35(3):272-80.
8. Semnani SH, Besharat S, Abdolahi N, Kalavi KH, Fazeli SA, Davarian A, et al. Esophageal cancer in northeastern Iran. Indian J Gastroenterol 2005;24:224.
9. O'Neill CH, Hodges GM, Riddle PN, Jordan PW, Newman RH, Flood RJ, et al. A fine fibrous silica contaminant of flour in the high esophageal cancer area of north-east Iran. Int J Cancer 1980;15:26(5):617-28.
10. American conference of governmental industrial hygienists. Documentation of the threshold limits values and biological exposure indices, sixth edition plus supplements 1991.
11. O'Neill C, Pan Q, Clarke G, Liu F, Hodges G, Ge M, et al. Silica fragments from millet bran in mucosa surrounding oesophageal tumours in patients in northern China. Lancet 1982;29:1(8283):1202-6.
12. Calvert GM, Rice FL, Boiano JM, Sheehy JW, Sanderson WT. Occupational silica exposure and risk of various diseases: an analysis using death certificates from 27 states of the United States. Occup Environ Med 2003;60:122-9.
13. Soutar CA, Robertson A, Miller BG, Searl A, Bignon J. Epidemiologiacal evidence on the carcinogenicity of silica: factors in scientific judgment. Annals of Occupational hygiene 2000;44:3-14.
14. Johnson WM, Busnardo MS. Silicosis following employment in the manufactures of silica flour and industrial sand. J Occup Med 1993;35(7):716-9.
15. Amre DK, Infante-Rivard C, Dufresne A, Durgawale PM, Ernst P. Case-control study of lung cancer among sugar cane farmers in India. Occup Environ Med 1999;56:548-52.