Selenium levels in rice samples from high and low risk areas for esophageal cancer

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ABSTRACT

Objectives: To assess the relationship between selenium (Se) concentration in rice and the incidence of esophageal cancer (EC) in a high risk area in Northern Iran.

Methods: This ecological study was conducted in Golestan province of Iran in 2012. In this area, 45714 acres of land are cultivated by rice. A total of 69 rice samples were taken. We investigated Se concentrations by the voltammetric method. Statistical analysis was performed using the Pearson correlation test and Mann-Whitney U test.

Results: The mean (±SD) Se level in rice samples was 0.229 (±0.145) mg/kg. The Se concentration was significantly higher in rice samples from high EC rate areas (0.35 mg/kg) compared with low risk areas (0.16 mg/kg) (p<0.001). There was a significant positive correlation between the levels of Se in rice and the incidence rate of EC (p=0.03).

Conclusion: We found a high rice Se concentration and a significant positive relationship between rice Se levels and EC rates in the Golestan province of Iran. High soil and rice Se levels may play a possible role in the pathogenesis of EC in this area.

Esophageal cancer (EC) is among eighth most common cancer in the world causing approximately 400,000 deaths in 2012.[1] Golestan province, in northeast Iran has been known as a high risk area for EC, most commonly esophageal squamous cell carcinoma (ESCC).[2] Esophageal cancer is a multi-factorial condition and various risk factors were proposed to play a role in its pathogenesis including high levels of selenium (Se) in serum[3] and soil[4] samples. Selenium is a metalloid and may be present in nature and in organisms as organic and/or inorganic forms. The essentiality and toxicity of Se are well known. Insufficient intake has been linked to serious health effects, such as dilated cardiomyopathy in Keshan disease, and osteoarthritis in Kashin-Beck disease.[5] However, high exposure to Se may be toxic to human beings.[6] The most important source of Se for animals and humans is food, especially cereals.[7] Rice is one of the commonly used cereals throughout the world. According to the Food and Agriculture Organization report,[8] almost 30% of energy, and 20% of the world's protein supply is provided via the use of rice. Rice is the main food in Asian countries including Iran. Golestan Province of Iran is considered an important area in rice cultivation. In view of the high usage of rice and the importance of EC in the Golestan province of Iran, we conducted this study to assess any relationship between rice Se concentration and the incidence of EC in this area.

Methods. *Collection of samples.* This ecological study was conducted in Golestan province in northern Iran between April 2012 and August 2012. The area under rice cultivation is 45714 acres. Rice is a major crop in this region. A total of 69 rice samples were collected from different regions of Golestan province (42 samples from low EC-risk areas and 27 samples from high EC-risk areas, based on rice cultivation in each area) (**Figure 1**). Samples were collected from rice

Figure 1 - Map of the Golestan province indicating the number of rice samples collected from different regions and cities. Reprinted from Semnani S, Roshandel G, Zendehbad A, Keshtkar A, Rahimzadeh H, Abdolahi N, et al. Soils selenium level and esophageal cancer: an ecological study in a high risk area for esophageal cancer. *J Trace Elem Med Biol* 2010; 24: 174-177, with permission from Elsevier.

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farms, put in impermeable plastic bags and kept in a refrigerator until analyzing.

Reagents. All reagents were of analytical grade. Deionized water was used in preparing stock solutions. All glass laboratory equipment were previously soaked in 30% nitric acid (HNO_3) (v/v) for 24 hours and rinsed with distilled water.

Sample preparation. The rice samples were washed with deionized water, and then were dried by oven at 60°C for 24 hours. The dried samples were milled to fine powder. From the milled rice, 1g was weighed and digested in a high-walled beaker with a mixture solution of HNO_3-H_2O_2. A sample of rice (1 g) and 5 mL HNO_3 (65%) were transferred into a 100 mL beaker and kept overnight. It was evaporated gently by using a hot plate until its volume reached approximately one-third of the original volume. Heating was continued until the evolution of brown fumes of nitrogen oxides ceased. Then, 2 mLs of H_2O_2 were added and heated again. This solution was cooled to room temperature and filtrated through a Whatman filter (0.45 µ), (GE health care, Little Chalfront, UK) into a 100 mL volumetric flask and filled to 100 mL with deionized water. Solutions were transferred to a polyethylene terephthalate bottle and were kept in a refrigerator until Se was measured using a polarograph, (Metrohm AG, Herisau, Switzerland).

Selenium determination by the voltammetric method. The voltammetric analysis[9] was carried out with a Metrohm 797 VA Computrace (Herisau, Switzerland). The 3 electrode classical cell consisted of an Hg electrode, a Pt electrode, and an Ag/AgCl reference electrode as well as a hanging mercury drop electrode (HMDE). Only high purity grade (Merck and Chem lab Suprapur, Darmstadt, Germany) reagents and deionized water were used. For calibration, the standard addition method[9] was applied. The calibration standards were prepared using Chem Lab, Zedelgem, Belgium at 1000 ppm of Se. The Se concentrations were quantified using linear regression based on the height of the peaks of the voltammograms.

Data were entered into a computer and statistical analysis was carried out using the Statistical Package for Social Sciences, version 16 (SPSS Inc., Chicago, IL, USA). Using the incidence rates of EC, Golestan province was divided into high and low risk areas for EC (**Figure 1**). Data on incidence rates of EC were obtained from the Golestan population-based cancer registry. Mann-Whitney U test was used to assess the difference in levels of Se between the 2 areas. Pearson's correlation tests were used to assess the correlation between mean rice Se levels and the incidence rates of EC in Golestan cities. A *p*-value of less than 0.05 was considered as significant. No human data or samples were collected in this study; therefore, there was no ethical consideration to be reviewed by our institutional ethical committee.

Results. In total, 69 rice samples were collected from different regions of Golestan province. Twenty-seven (39.1%) of the samples were collected from low EC-risk areas, and 42 (60.9%) from high EC-risk areas (**Figure 1**). An internal quality control of the analytic procedure was conducted throughout the study. Accuracy was evaluated by adding the standard Se (5 µg/l) into the sample, the mean recovery was 98.1% (93.7-105.4%). The coefficient of variation obtained was 2.8%. The maximum concentration of Se in rice samples was 0.5 mg/kg. The mean (SD) level of Se in rice samples in the low EC-risk area was 0.16 mg/kg (±0.02), and in high EC-risk area was 0.35 mg/kg (±0.02) ($p<0.001$). We also found a significant correlation between rice Se levels and the incidence rate of EC in Golestan province (Pearson's correlation coefficient=0.65, $p=0.03$) (**Figure 2**).

Discussion. We found a relatively high concentration of Se in rice samples from the Golestan province of Iran (0.229 mg/kg). The mean Se content values in rice reported in literature were 0.020 mg/kg for Italy in 2007,[10] and 0.05 mg/kg for Korea in 2004.[11] Our results also suggested that the level of Se in rice samples from high EC-risk areas was significantly

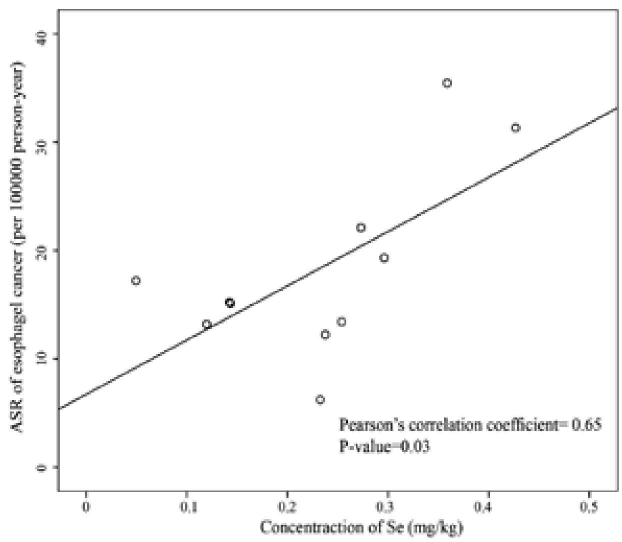

Figure 2 - Correlation between age standardized incidence rate (ASR) of esophageal cancer and mean selenium (Se) concentrations in rice samples from Golestan cities, Iran.

higher than low risk areas. In some studies, Se has been investigated in relation to cancer risk due to its protective effects. Some studies have found Se status to be inversely associated with cancer risk. Negative associations have been found for various parameters of Se status and risks to cancers.[12]

Selenium was suggested as a possible factor in the regional variation of cancer mortality in China and other areas, specifically for EC.[13] Similar results were reported on the levels of Se in soil samples from Golestan province.[4] Semnani et al[4] in 2010 reported a significantly higher level of soil Se in high EC-risk areas than low EC-risk areas and suggested soil Se level as a possible risk factor for EC in this region. Therefore, rice Se levels may be considered a possible contributor to the high incidence of EC in Golestan province.

The results of the present study were in line with those from previous studies,[4] suggesting that contamination of the environment (soil, rice, and so forth) by xenobiotics including Se may be proposed as a possible risk factor for EC in this region. Therefore, it should be considered in designing cancer control programs in this area.

We found a significant correlation between the levels of Se in rice samples from Golestan province and the incidence rate of EC in this region. Soils contaminated by xenobiotics from aerial depositions and irrigation are likely to induce a corresponding contamination in harvested crops. Crops grown on contaminated land can carry pollution to humans or animals.[14] However, farmers use chemical fertilizers for fertilization of products, and this may lead to the accumulation of xenobiotics in rice.[15] Accordingly, one of the main routes for human exposure to xenobiotics is the soil-crop-food pathway.[14] There may be a direct relationship between the composition of soil including xenobiotics and that of agricultural products such as rice. Therefore, environmental characteristics (for example, soil composition) should be closely monitored especially in high risk areas including Golestan province of Iran. Any change or abnormality should be considered an important health-related issue and should be addressed in health policy-making and control programs.

This study suffers from limitations of ecological designs including the ecologic fallacy of assumed equal exposure, and the absence of temporal relationship between exposure and outcome. So a causal relationship could not be concluded from our findings. Further individual-based studies are needed to determine the role of Se in the pathogenesis of EC in this region.

In conclusion, our results showed high levels of Se in rice samples and a significant positive relationship between rice Se levels and EC rates in the Golestan province of Iran. Considering the previously reported correlation between soil Se levels and EC rate, it may be concluded that high soil and rice Se levels may play a possible role in the pathogenesis of EC in this area.

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