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Plasma Selenium Measurements in Subjects from Areas with Contrasting Gastric Cancer Risks in Colombia

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Background. An inverse association between selenium status and incidence of different neoplasias including gastric cancer has been reported. This pilot study aimed to determine and compare selenium status in two Colombian populations with different gastric cancer risks: a high-risk area in the volcanic region of the Andes Mountains and a low-risk area on the Pacific coast.

Methods. Eighty nine adult males were recruited in the outpatient clinics of two public hospitals (44 and 45 from high- and low-risk areas, respectively) and provided a blood sample. Seventy one (79.8%) participants underwent upper gastrointestinal endoscopy. Plasma selenium was assayed using a fluorometric method, selenoprotein-P by ELISA, and glutathione peroxidase activity by a spectrophometric method. Histological diagnosis and *Helicobacter pylori* infection were evaluated in gastric biopsy samples. Unpaired samples *t*-test and linear regression analyses were used for statistical analyses.

Results. Although none of the subjects in either of the two geographic areas was selenium deficient, the level of plasma selenium was significantly lower in men from the high-risk area compared with those from the low-risk area. Levels of selenoprotein-P and glutathione peroxidase activity were similar between groups after adjustment for confounders. Selenium measurements were not associated with histopathological diagnosis.

Conclusions. The high incidence of gastric cancer in the Andean region of Colombia is unlikely to be explained by selenium deficiency. We cannot exclude, however, that suboptimal selenium levels may exist in the gastric mucosa of subjects in the high-risk area. Therefore, the benefit of selenium supplementation in gastric cancer prevention cannot be dismissed.

Key Words: Selenium, Selenoprotein-P, Glutathione peroxidase, Gastric cancer risk.

Introduction

Cancer of the stomach is the second most common cause of death from cancer and the fourth most common cancer worldwide. Incidence varies greatly among populations and is higher in Asian, Central and South American countries, and lower in North America and Western Europe (1,2). In Latin America, high-risk pockets are found in the high altitude Andean regions where volcanoes abound (2). Migration studies reporting dramatic decreases in gastric cancer within one generation in subjects who have moved from areas of high to low incidence suggest that environmental factors may be involved in its etiology (3,4).

Selenium (Se) is an essential dietary nutrient for all mammalian species. Two selenoproteins, extracellular glutathione peroxidase (GPx3), and selenoprotein P (Sepp1),

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apparently exert antioxidant effects (5,6). Although several epidemiological studies have reported that subjects who develop cancer are Se deficient, the evidence is not consistent (7). With respect to gastric cancer, ecological studies conducted in areas of high gastric cancer risk in Asia showed a significant inverse correlation between gastric cancer mortality and Se in drinking water (8) or with plasma Se (9). Four large-scale cohort studies have reported statistically significant inverse associations (10–13). Three case-control studies observed no associations between Se and gastric cancer risk or precancerous lesions (14–16). Regarding randomized intervention trials, two studies found no association between a vitamin/mineral dietary supplement and gastric cancer risk. Given that those trials examined the effect of Se in combination with other micronutrients, inferences regarding the individual effect of Se cannot be drawn (17,18). However, a double-blind, randomized trial showed a reduced risk of gastric cancer in individuals supplemented with a combination of Se, β-carotene, and α-tocopherol (19).

The mechanism behind the putative beneficial effect of Se is believed to be its ability to act as an antioxidant, mainly through prevention of cellular proliferation and through inhibition of cellular damage by free radicals (20). Because many selenoproteins have been shown to have antioxidant activity (21), higher intake of Se may lead to increased expression of selenoproteins; hence, protecting DNA against oxidative damage.

Our previous long-term research in Colombia has identified in the south of the country (State of Nariño) two areas with contrasting gastric cancer risks: a high-risk area in the volcanic region of the Andes Mountains and a low-risk area on the Pacific coast. This difference in cancer incidence persists, although residents of these areas have a similarly high prevalence of infection with *Helicobacter pylori* (22,23), a major environmental gastric carcinogen (24). Because Andean regions commonly have volcanic soil with low Se content (25,26), we hypothesized that plasma Se levels would be different between these populations, especially in those individuals suffering from any *H. pylori*-associated gastric diseases. This pilot study aimed to measure Se, GPx activity, and Sepp1 levels in plasma from men from the above-mentioned areas and to determine differences between them.

Materials and Methods

Study Population

Eighty nine adult males between 31 and 60 years old with dyspeptic symptoms who attended the gastroenterology outpatient clinics of two public hospitals between August and November of 2006 in the towns of Tuquerres and Tumaco were enrolled in this study and provided informed consent. Of these, 71 individuals underwent diagnostic endoscopy of the upper gastrointestinal tract. All participants were born in the studied areas and had lived in those areas for decades (median 40 years). Exclusion criteria included previous gastrectomy, concomitant major diseases (i.e., cancer, cardiac failure), and intake of H_2-receptor antagonists, proton pump inhibitors, or antimicrobials in the 4 weeks prior to the endoscopic procedure. Forty four of the males were residents of the area of high gastric cancer risk and 45 were from the low-risk area. The high-risk area of Tuquerres (estimated incidence rate of 150/100,000 in 1976) in the volcanic region of the Andes Mountains is located at 3000 m above sea level. Its inhabitants are of mixed Spanish and Amerindian ancestry and have an agriculture-based economy. In the low-risk area of Tumaco on the Pacific coast (estimated incidence rate of 6/100,000 in similar coastal areas in 1976) (27), the population is of Spanish-African ancestry and the economy is based on fishing. These areas are about 143 miles apart. The proposal for this study was approved by the Ethics Committee of the Universidad del Valle and the two local hospitals.

Histopathology

During endoscopy, at least three gastric mucosa biopsies were obtained from each patient: one from the antrum (greater curvature, within 5 cm of the pylorus), one from the lesser curvature (at the incisura angularis), and one from the corpus (middle anterior wall). Gastric biopsies for histology were fixed in buffered formalin and embedded in paraffin. Four-μm-thick sections were stained with hematoxylin and eosin for histopathological diagnosis and with modified Steiner silver stain (28) for evaluation of *H. pylori* infection.

Histopathological diagnoses were independently assessed by two experienced pathologists (PC and MBP) according to established guidelines (29,30) as follows: normal, non-atrophic gastritis (NAG), multifocal atrophic gastritis without intestinal metaplasia (MAG), intestinal metaplasia (IM), and dysplasia (DYS). Cases with discordant diagnoses were reviewed in a double-headed microscope and a consensus was reached. Pathologists were blinded to the site of residence of the participants and to the Se profile results.

Plasma Selenium Measurements

Blood specimens were obtained from participants by venipuncture. A 5-mL blood sample was obtained and treated with EDTA to prevent coagulation. Plasma was separated by centrifugation within 30 min after the sample was taken and stored in a liquid nitrogen tank. Later, the samples were placed in a −70°C freezer. Samples were labeled in Colombia and shipped frozen in dry ice to Vanderbilt University, Nashville, Tennessee.

Reagents for biochemical analysis obtained from Fisher Scientific (Pittsburgh, PA) were of analytical grade or better. The source of specialty chemicals is listed with each