SHORT REPORT

Low selenium levels in serum and increased concentration in neoplastic tissues in patients with colorectal cancer: Correlation with serum carcinoembryonic antigen

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Introduction

There is growing evidence to show that administration of selenium (Se) is associated with a substantial reduction in the incidence and mortality of various cancer types such as skin, prostate, lung, and colorectal cancer (CRC) as well as in sarcomas in both animals and humans [1,2]. Epidemiological studies have shown a reduced risk for the same neoplasms for people living in geographic areas with comparatively high soil Se levels. Similarly, epidemiological and experimental studies suggest an inverse relationship between intake of dietary Se and/or a low-fat intake and CRC risk [3]. CRC is one of the leading causes of cancer-related deaths. Approximately 95% of cases are sporadic. Early detection and prevention are the two most important considerations facing CRC. Low Se intake and plasma levels have been implicated in the multi-step process of colorectal carcinogenesis. However, their relationship remains elusive and intriguing [3–5]. There are studies suggesting that selenium supplementation decreases the cyclooxygenase-2 (COX-2) protein and PGE-2 levels in cancer cells and increases the efficacy of cetuximab in patients with advanced CRC [6–8].

Material and methods

Participants

In all, 120 patients (70 M, 50 F, mean age 60.5 years, age range 36–82 years) suffering from CRC were included in the study.

Methods

Serum Se (Table I) and carcinoembryonic antigen (CEA) levels were measured in all patients. Patients underwent colectomy and Se concentration in neoplastic and non-neoplastic tissue specimens – taken at a distance of at least 5 cm from the tumor mass – was calculated (Table I). Se levels in normal Greek individuals were determined using a control group consisting of 500 age-matched, healthy individuals (250 M, 250 F) (Table I). Se concentrations in serum, and cancerous and healthy tissues were determined using a fluorometric assay as described previously [3,4] and are presented in Table I.

Results

We found a statistically significant decrease in serum Se levels in patients suffering from CRC compared...
to normal individuals (40 ± 7.8 µg/l and 66.6 ± 7.2 µg/l, respectively, p < 0.001). Conversely, Se concentration in the cancerous tissue was significantly increased compared with that in healthy tissue (2580 ± 230 µg/g tissue and 690 ± 120 µg/g tissue, respectively, p < 0.001). Serum CEA levels in patients with CRC were 15 ± 3.3 U/ml (normal 1–5 U/ml). A statistically significant relationship between CEA and Se levels was found (r = −0.764, p < 0.001).

### Comments

To the best of our knowledge the present study is the second one providing information on neoplastic tissue Se concentration in CRC patients and the first study to provide data for serum/tissue Se concentrations simultaneously in association with serum CEA levels. Our findings regarding serum Se levels in patients suffering from CRC are in agreement with other reports in patients with lung, gastric, and renal cancer and CRC [1,4]. It is not clear whether the increased Se concentration in the cancerous tissue is responsible for the decreased serum Se levels found in these patients or whether the decreased serum Se levels precede the development of CRC. The existing studies do not shed any light on this issue since the reports on colorectal adenomas, the known precursors of CRC, are controversial [4,5]. Another consideration is the significance of the increased Se concentration in neoplastic tissue. An attractive hypothesis is that it is part of the defense mechanisms against the neoplastic process. This concept is supported by the known antioxidant action of Se. Selenomethionine (SeMet) might affect colon cancer growth by mechanisms involving cyclooxygenase (COX). Other selenoproteins such as glutathione peroxidase (GPx), thioredoxin reductase (TrxR), and selenoprotein P (SeP), which contain molecular Se in the form of selenocysteine within their active center, act similarly. Through these selenoproteins, Se regulates the cellular antioxidant defense system, DNA damage and protein function. In addition, Se controls cell-mediated immunity and B-cell function.

The inverse relationship between Se and CEA serum levels demonstrated here possibly indicates that the development and progression of CRC are associated with decreasing levels of serum Se. Of course, further studies with larger series of patients are needed in order to clarify this hypothesis.

### References


