Original Article

Plasma vitamin A and E levels in patients with gastroesophageal cancer in Eastern Anatolia

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Aim: Gastrointestinal system (GIS) cancers account for a significant percentage of morbidity and mortality worldwide. Free radicals may play a role in the development of GIS cancers at various stages. The goal of this study was to analyze the relationship between gastroesophageal cancer and plasma levels of vitamin A and vitamin E, a significant part of antioxidant defense.

Materials and methods: Twenty-six patients with gastroesophageal cancer diagnosed by endoscopy and histopathologic examination and 26 healthy volunteer subjects were included in this study. Plasma vitamin A and vitamin E levels were determined by high-performance liquid chromatography using a commercially available kit.

Results: Plasma vitamin A and vitamin E levels were significantly lower in the gastroesophageal cancer group (1.39 ± 0.137 µmol/L and 13.5 ± 1.29 µmol/L, respectively) than in the control group (2.79 ± 0.163 µmol/L and 21.29 ± 2.58 µmol/L, respectively). The difference was significant at $P < 0.001$ for vitamin A, and $P < 0.05$ for vitamin E values. However, we could not detect any significant difference in plasma vitamin A and vitamin E levels when the stage of the disease was taken into consideration ($P > 0.05$).

Conclusion: Decreased plasma vitamin A and vitamin E levels, as important antioxidant components, may be contributory in the development of gastroesophageal cancer. Diets rich in antioxidant vitamins may be protective against the development of upper gastrointestinal tract disease.

Key words: Vitamin A, vitamin E, gastroesophageal cancer, oxidative stress

Doğu Anadolu'da gastroözofageal kanserli hastalarda plazma vitamin A ve E düzeyleri

Amaç: Gastrointestinal sistem (GIS) kanserleri dünya çapında önemli morbidite ve mortalite nedenleridir. Serbest radikaller farklı evrelerdeki GIS kanserlerinin gelişiminde rol oynayabilirler. Bu çalışmanın amacı antioksidan savunmanın önemli bir parçası olan vitamin A ve E nin plazma düzeyleriyle gastroözofageal kanserler arasındaki ilişkiyi analiz etmektir.

Yöntem ve gereç: Çalışmaya endoskopik ve histopatolojik olarak tanı konmuş 26 gastroözofageal kanserli hasta ve 26 sağlıklı gönüllü dahil edildi. Plazma vitamin A ve E düzeyleri high-performance liquid chromatography (HPLC) yöntemi (HP 1100 kitleri) ile ölçüldü.

Bulgular: Plazma vitamin A ve E düzeyleri gastroözofageal kanserli hastalarda (sırasıyla 1,39 ± 0,137 µmol/L and 13,5 ± 1,29 µmol/L) kontrol grubuna (sırasıyla 2,79 ± 0,163 µmol/L and 21,29 ± 2,58 µmol/L) göre belirgin derecede düşük bulundu. Fark vitamin A için P < 0,001 ve vitamin E için P < 0,05 olarak anlamı tespit edildi. Buna rağmen hastalığın evresiyle plazma vitamin A ve E düzeyleri arasında ilişki saptanamadı (P > 0,05).

Sonuç: Önemli antioksidan komponentlerden vitamin A ve E'nin plazma düzeylerindeki azalma, gastroözofageal kanser gelişmesine katkıda bulunabilir. Antioksidan vitaminlerden zengin besinlerin tüketilmesi, üst gastrointestinal sistem kanseri gelişmesine karşı koruyucu olabilir.

Anahtar sözcükler: Vitamin A, vitamin E, gastroözofageal kanser, oksidatif stres

Introduction

Under normal circumstances, free radicals are kept in balance by detoxification via the intracellular and extracellular antioxidant defense mechanism (1). An excessive increase in the level of free radicals in the body and insufficiency in the antioxidant system may play a significant role in the occurrence of heart failure, cerebrovascular diseases, and a number of other diseases, such as cancer (2). Moreover, apart from inflammation, radiation, and mutagenic chemicals, an increase in free oxygen radicals may cause DNA (deoxyribonucleic acid) damage, mutations, and chromosome aberrations and play a role in some stages of carcinogenesis (3,4). Antioxidant vitamins have long been considered to contribute to reducing the risk of cancers at many sites. In particular, it has been hypothesized that the antioxidant activity of vitamins may be protective against gastrointestinal cancer. Antioxidants inhibit DNA synthesis, inhibit cell transformation, change gene expression, decrease cell proliferation, and protect against oxidative stress (5).

The most constant finding in the relation between diet and gastrointestinal cancer is the protective effect of vegetables and fruits. A large number of potentially anticarcinogenic agents are found in these food sources, such as vitamin A, vitamin E, and carotenoids (6).

In this study, we aimed to determine the relationship between the plasma levels of vitamin A and vitamin E, which are a significant part of the antioxidant defense system and have a protective effect against free radicals in cancer development, and stomach and esophageal cancer.

Materials and methods

A total of 52 people, comprising 9 with esophagus adenocarcinoma (5 females, 4 males), 17 with stomach adenocarcinoma (8 females, 9 males), and 26 completely healthy individuals, were included in our study. The mean ages of patients at cancer diagnosis and of control subjects were 62 years (41-87) and 58 years (31-77), respectively. All of the patients were examined with imaging methods (ultrasonography-computerized tomography), and their stage studies were carried out according to TNM (tumor, lymph node, metastasis) classification (7). According to this classification, 17 were in stage III and 9 in stage IV.

Venous blood from all individuals was taken antecubitally into 5 mL EDTA (ethylene diamine tetra acetic acid)-containing tubes. Patients were in a fasting state, and blood was collected in the morning. The plasma of the collected blood was separated by centrifuging for 10 min at 2500 rpm at +4 °C. The separated plasma was immediately stored in Eppendorf tubes at -80 °C in the dark.

Determination of plasma vitamin A and E levels

Plasma vitamin A and E levels were determined by high performance liquid chromatography (HPLC) (HP 1100), using a Chromsystems analytical column (Chromsystems Instruments and Chemicals GmbH, Munich, Germany) and mobile phase and other reagents and standards provided by the same company (8). The instrument parameters were: injection volume 50 mL, analytical run time 15-17 min, light-protected sample, flow rate 1.5 mL/min, and column temperature 20 °C. The UV detector l was initially set at 325 nm and switched to 295 nm after 3 min.

Statistical analysis

Data were analyzed by the Mann–Whitney U and Fisher's exact tests, using SPSS (Statistical Package for the Social Sciences) 10.0 for Windows (SPSS, Chicago, IL, USA). In order to assess the correlation between age of patients with gastroesophageal cancers and plasma vitamin A and E levels, Pearson's correlation analysis was used. The statistically significant probability level was set at 0.05. The results are given as mean ± standard deviation (X ± SD).

Results

Plasma vitamin A levels in 10 of 26 patients were found to be below normal, while vitamin E levels in 13 patients were below normal. The mean value of plasma vitamin A in the patient group was 1.39 ± 0.137 µmol/L (control group 2.79 ± 0.163 µmol/L), and that of plasma vitamin E was 13.5 ± 1.29 µmol/L (control group 21.29 ± 2.58 µmol/L). In comparison to the control group, there was a statistically significant difference in the plasma vitamin A and E levels of the patient group (P < 0.001 and P < 0.05, respectively) (Table).

Six of the patients whose plasma vitamin A levels were below normal levels were stage III and 4 were in stage IV. Of the patients with normal plasma vitamin A levels, 11 were stage III and 5 were stage IV. We did not find any relationship between plasma vitamin A values and the stage of the patients with gastroesophageal cancer (P = 0.69) (Figure 1).

Ten of the patients whose plasma vitamin E levels were below normal were in stage III and 3 were in stage IV. Of the patients with normal plasma vitamin E levels, 7 were in stage III and 6 were in stage IV. We did not determine any relationship between plasma vitamin E values and the stage of the patients with gastroesophageal cancer (P = 0.41) (Figure 2).

Discussion

Under oxidative stress, excessive production of free oxygen radicals or disability in antioxidant systems may occur. The fact that oxidative stress has a significant role in cancer development has been shown in several published studies (3,9). Nutritional factors are thought to be paramount, with N-nitroso and other dietary compounds acting as carcinogens, while antioxidants and other protective substances in foods inhibit the carcinogenic process (6).

Table. Vitamin A and E levels (mean ± SD) in patient and control groups.

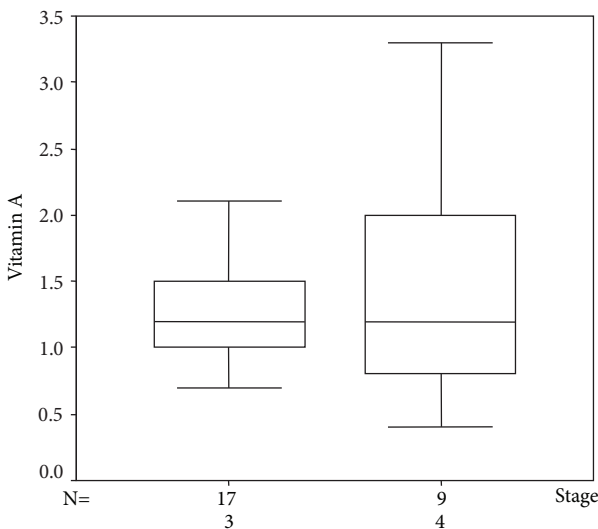|	Control group	Gastroesophageal cancer	
Cases (n)	26	26	
Age (year)	58 ± 9.36	62.1 ± 10.67	
Vitamin A (µmol/L)	2.79 ± 0.163	1.39 ± 0.137	P < 0.001
Vitamin E (µmol/L)	21.29 ± 2.58	13.5 ± 1.29	P < 0.05

Figure 1. Relationship between plasma vitamin A levels and stage of gastroesophageal cancer (P > 0.05).
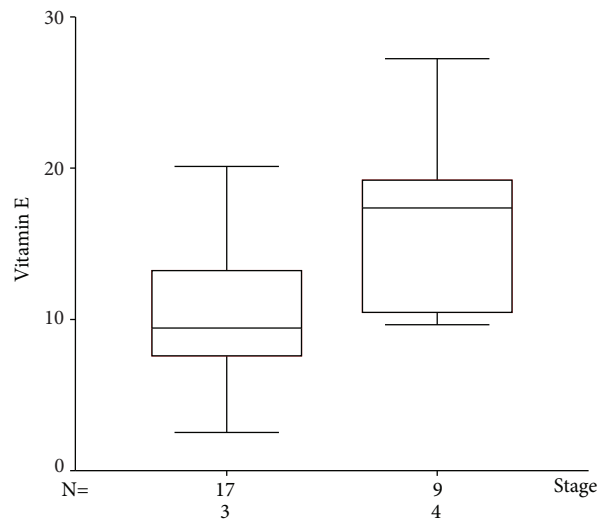

Figure 2. Relationship between plasma vitamin E levels and stage of gastroesophageal cancer (P > 0.05).

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Vitamin A is also a well-known antioxidant, but its protective effect against gastric cancer has rarely been reported (10). Vitamin E has some known or presumed functions in addition to being an antioxidant that may have a part in inhibiting carcinogenesis. Results of chemical carcinogenesis studies in rodents suggest that vitamin E inhibits the development of cancer at many sites, and the results of prospective cohort studies and randomized intervention trials in humans have also provided some evidence that vitamin E plays a role in the prevention of gastroesophageal cancers (11). Zhang (12) described the beneficial effects of vitamin E in relation to adenocarcinoma development. Thus, the serum levels of these antioxidant vitamins are considered to reflect the antioxidant status of the body involved in the process of carcinogenesis (13).

In China, 29,584 participants were sampled from the general population of Linxian. This trial tested 4 different combinations of nutrient supplements for 5.25 years. The group supplemented with selenium, ß-carotene, and vitamin E had a statistically significant reduction of 13% in cancer mortality (5). In another study carried out in the same country, the levels of vitamin C and serum β-carotene in individuals with intestinal metaplasia, which is a gastric precancerous lesion, were significantly lower than in individuals with normal gastric mucosa (14). One study from Sweden evaluated the association between the intake of antioxidants (vitamin E and β-carotene) and esophageal cancers, and reported that these nutrients are inversely associated with the risk of carcinoma of the esophagus (15).

In Italy, in a study of 382 patients with stomach cancer, the intake of high-doses of a-tocopherol was found to prolong life expectancy. In contrast to other reports in the literature, that study was unable to determine the effectiveness of other antioxidants (16).

Stahelin et al. (17) examined antioxidant vitamin values in 2974 individuals. During his 12-year follow-up, 204 of them died from cancer. In those who died, especially those who died of stomach cancer, plasma carotene levels were found to be low (P < 0.01). Knekt et al. (18) measured the levels of serum a-tocopherol in 36,265 people and followed them for 8 years to determine who developed cancer. A reverse correlation between serum vitamin E levels and cancer development was found, which was particularly striking in gastrointestinal cancers. The incidence of cancer was 1.5 times greater in those whose serum a-tocopherol levels were low, supporting the hypothesis that dietary intake of vitamin E is protective against cancers.

Tsubono et al. (19) examined 634 individuals from 5 different Japanese populations in which mortality rates from stomach cancer varied, and found that the levels of plasma b-carotene and a-tocopherol are inversely related to the incidence of stomach cancers.

In our study of vitamin A and E levels, the distinction between the patient and control groups is statistically significant. While there is a significant difference between healthy controls and patients with gastroesophageal cancers in terms of plasma vitamin A and E levels, no significant difference was determined in vitamin A and E levels between cancer patients according to cancer stage III or IV.

Our results, indicating low plasma vitamin A and E levels in patients with stomach and esophageal cancers, support the possibility that the lack of antioxidant vitamins is a significant etiologic factor. But is the vitamin deficiency in these patients a cause or a result? The poor nutritional status of cancer patients is a known fact. Thus, as the stage of the disease progresses, we could expect that any deficiency in antioxidant vitamins would increase. Nevertheless, in our study we were unable to determine any significant difference in plasma vitamin A and E levels between patients with cancer stage III or IV. This would suggest that the deficient levels of plasma vitamin A and E in our patients were a cause.

In summary, our results confirm the important role that diet plays in the etiology of gastroesophageal cancer. Diets rich in vegetables, fruits, vitamins, and antioxidants may be a protective factor against stomach and esophageal cancers. Further studies are necessary to clarify whether additional vitamin supplementation can reduce the risk of gastroesophageal cancers.

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