Turk J Gastroenterol 2003; 14 (1): 50-53

Dietary nitrate and nitrite levels in an endemic upper gastrointestinal (esophageal and gastric) cancer region of Turkey

Türkiye'nin endemik üst gastrointestinal (özofagus ve mide) kanser bölgesinde diyetde nitrat ve nitrit düzeyleri

M.Kürşat TÜRKDOĞAN[1], Haluk TESTERECİ[2], Nevzat AKMAN[3], Tahir KAHRAMAN2, Kazım KARA[4], İlyas TUNCER[1], İsmail UYGAN[1]

Yüzüncü Yıl University School of Medicine, Division of Gastroenterology[1], Faculty of Veterinary, Department of Biochemistry[2], School of Medicine, Department of Public Health[3], Department of Biometry and Genetics, Faculty of Agriculture[4], Van

Background/aims: *The aim of this study was investigate nitrate and nitrite levels in some traditional foods and drinking water in Van, an endemic upper gastrointestinal (esophageal and gastric) cancer region of Eastern Turkey.* ***Methods:*** *Cheese with added herbs, drinking water, bread baked by wood fire and bread baked by burning animal manure specimens collected in the Van region were analyzed by Stahr's modification method. Nitrite was reduced to nitrate by the following three reagents: hydrazine sulphate ((NH_2) 2SO4), CuSO4 and NaOH. Nitrate was then determined by coupling reagent containing sulphanlyamide, phosphoric acid and N-1-naphtyl ethylendiamine dihydrochloride.* ***Results:*** *Nitrate and nitrite levels of all traditional foods and nitrite levels of drinking water were very significantly elevated compared to standard values (p<0.001-0.01).* ***Conclusions:*** *These findings suggest that the influence of a traditional diet rich in nitrate and nitrite is significant in the development of endemic upper gastrointestinal (esophageal and gastric) cancers in the Van region of Turkey.*

Key words: Nitrate, nitrite, esophageal and gastric cancer, Eastern Turkey

Amaç: *Endemik üst gastrointestinal (özofagus ve mide) kanser bölgesi olan Van'da sık olarak yenilen bazı geleneksel besinler ve içme suyunda nitrat ve nitrit düzeyleri araştırılması amaçlanmıştır.* ***Metod:*** *Van bölgesinde otlu peynir, içme suyu, odun ateşi ve tezek (hayvan atığı) ateşinde pişen ekmek örneklerinde nitrat ve nitrit düzeyleri Stahr modifikasyon yöntemi ile ölçüldü. Nitritin nitrata indirgenme işlemi hydrazine sulphate ((NH_2) 2SO4), CuSO4 and NaOH gibi üç ayıraç ile yapıldı. Daha sonra nitrat düzeyleri sulphanlyamid, phosphoric acid ve N-1-naphtyl ethylendiamin dihydrochloride içeren indirgeyici ayıraç ile belirlendi.* ***Bulgular:*** *Tüm geleneksel besinlerde nitrat ve nitrit düzeyleri, içme suyunda ise nitrit düzeyleri kontrol değerlerine göre ileri derecede anlamlı yüksek bulundu (p<0.001- 0.01).* ***Sonuç:*** *Bu bulgular Van bölgesinde nitrat ve nitritden zengin geleneksel diyetin üst gastrointestinal (özofagus ve mide) kanserlerin gelişmesinde önemli rolünü ortaya koymaktadır.*

Anahtar kelimeler: Nitrat, nitrit, özofagus ve mide kanserleri, Doğu Anadolu

INTRODUCTION

Gastrointestinal (GI) cancers are a significant and often fatal health problem throughout the world. In the United States, 20% of all cancer deaths are gastrointestinal cancers (1). In the eastern Anatolian region of Turkey, upper gastrointestinal cancers (esophageal and gastric) are the main cause of morbidity and mortality among all cancer types (2,3) and many ecological risk factors, especially dietary habits, play an important role in the etiopathogenesis of these cancers (4). In this study, the dietary nitrate and nitrite levels in some traditional foods (herb - enriched cheese, bread baked by burning animal manure or by wood fire) and in frequently consumed drinking water was investigated in the Van region of eastern Turkey.

MATERIALS AND METHODS

Fifty 150 g samples of herb- enriched cheese (HC), 30 x 500 ml samples of drinking water (DW), 35 samples of bread baked by wood fire (BW) and 25 samples of bread baked by burning animal manure (BAM) were collected randomly in the residential districts of upper GI cancer patients in the Van region. All samples of the herb-enriched cheese and the bread were home made. The nitrate and nitrite levels of all specimens were analyzed by Stahr's modification method (5). In this method nitrite was reduced to nitrate by the following three reagents: hydrazine sulphate ($(NH_2)_2SO_4$), $CuSO_4$ and NaOH. The nitrate level was then determined by coupling reagent containing sulphanlyamide, phosphoric acid and

Address for correspondence: Doç. Dr. M. Kürşad Türkdoğan
Yüzüncü Yıl Üniversitesi Tıp Fakültesi İç Hastalıkları ABD
65200 Van, Turkey
Fax: +90 432 2168352
E-mail: mkturkdogan@yahoo.com

Manuscript received: 2.7.2002 **Accepted:** 7.1.2003

N-1-naphtyl ethylendiamine dihydrochloride. Standard calibration solutions were prepared by dilution of standard potassium nitrate solution (1000ppm). Ten grams of each sample were dissolved in 100 ml of water, mixed for 35 minutes and the filtered liquid was then used for nitrate analysis. Water samples were used directly without dilution. For the nitrate measurement a 3ml sample of liquid was mixed with 1ml of coupling reagent and, mixed for 10 minutes and read at 520 nm light. Reduction of nitrite to nitrate was unduced by the addition of 1ml of (NH_2) $2SO_4$, $CuSO_4$ and NaOH to 1ml of sample liquid (or standard). After waiting 10 minutes for the reduction of nitrite to nitrate, nitrate measurement was undertaken. Required corrections were made for the conversion of nitrite to nitrate, percentage of dry weight and dilution factors. The amount of nitrite and nitrate were calculated using standard calibration graphic via regression analysis.

The standard nitrate and nitrite values of foods (cheese, drinking water, bread etc.) were reported in the literature (6,7). The nitrate and nitrite values of samples in this study were compared to standard values (S) by "Student's one sample t" test.

RESULTS

Mean nitrate and nitrite levels of traditional foods and drinking water in the Van region and standard values (S) are presented in Table 1. Mean nitrate and nitrite levels of herb-enriched cheese (HC) were significantly higher than standard values ($p<0.001$). The mean nitrite level was significantly high ($p<0.05$) and nitrate level was very high ($p<0.001$) in bread baked by wood fire (BW). In bread baked by burning animal manure (BAM), mean nitrate and nitrite levels were also significantly elevated ($p<0.001$) and the levels tended to be higher than bread baked by wood fire levels. In drinking water (DW), the mean nitrite level was also significantly higher ($p<0.01$) while the nitrate level was significantly lower ($p<0.001$), suggesting a reduction of nitrates to nitrites due to bacterial overgrowth.

The comparison of mean nitrate and nitrite levels of traditional foods and drinking water in the Van region with standard values (S) are presented in Figure 1 and Figure 2.

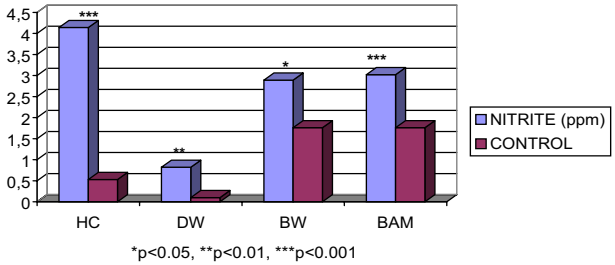


Figure 1. Nitrite levels of traditional foods and drinking water in Van region.

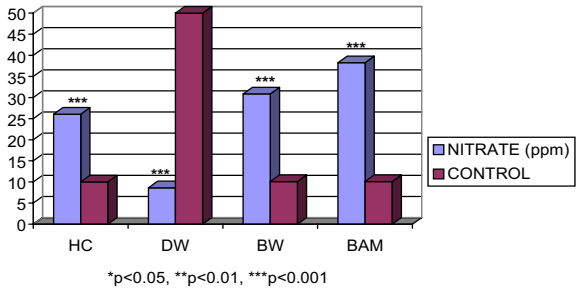


Figure 2. Nitrate levels of traditional foods and drinking water in Van region.

Table 1. Nitrate and nitrite levels of traditional foods and drinking water in Van region and standard values (S).

FOODS AND WATER	NITRITE (ppm)					NITRATE (ppm)			
	N	X±SE	Min	Max.	S	X±SE	Min	Max.	S
Herb-enriched cheese	50	4.14±0.50***	0.67	18.53	0.53	26.06±3.14***	7.31	107.57	10.00
Drinking by	30	0.82±0.22**	0.00	6.40	0.10	8.62±0.77***	2.14	18.61	50.00
Bread baked by wood fire	35	2.89±0.51*	0.40	15.40	1.76	30.87±3.26***	7.09	85.74	10.10
Bread baked by animal manure	25	3.02±0.19***	1.60	5.60	1.76	38.25±3.70***	8.21	83.97	10.10

*p<0.05, **p<0.01, ***p<0.001
SE: Standard error, S: Standard values

DISCUSSION

In the Van region of Turkey, there are many ecological risk factors in the etiopathogenesis of upper GI cancers including radioactivity, heavy metals, asbestosis but traditional dietary factors seem to be the most important. In underdeveloped rural areas of the Van region and in Eastern Turkey generally, animal manure is widely used as a fuel for baking and roasting foods such as bread and meat in a traditional smoke filled large oven (3). Also, the consumption of salted, fried lake fish and regional herb-enriched cheese rich in nitroso compounds is traditional in the Van region and the analysis of well water in rural endemic areas has revealed high nitrate and nitrite levels (8). In a previous study, the present authors also detected that serum nitrate and nitrite levels were significantly elevated in gastric cancer patients with H.pylori infection in the Van region (9).

In this study, the nitrate and nitrite levels of some traditional foods and drinking water were investigated and found to be significantly elevated compared to standard values. Nitrate and nitrite levels of bread baked by burning animal manure tended to be higher than those of bread baked by wood fire, suggesting the risk of this widespread practice in rural endemic cancer areas of Eastern Turkey. These home smoked foods also have potent carcinogenic properties due to their high benzapyrene levels as reported in some other studies (10). The significantly high nitrite level of drinking water in the Van region suggests bacterial contamination and this finding is an additional carcinogenic risk factor.

Gastrointestinal (GI) cancers are an important cause of morbidity and mortality throughout the world. Of all cancer, GI cancer has the highest prevalence (27) in Eastern Turkey, with upper GI (esophageal and gastric) cancers being the most frequent and fatal group with the highest endoscopic prevalence (1-7) in the Van region (2).

It has been established that there is an “upper GI (esophageal and gastric) cancer belt”, originating in the Far East (Japan, Korea, China) and extending through Middle Asian countries (Uzbekistan, Turkmenistan etc.) as far as the Near East (Iran, Caucasian and Eastern Anatolia regions of Turkey). In these endemic upper GI cancer regions, the people are of low socioeconomic status and have poor nutritional habits (home smoked and salty foods, hot tea consumption, lack of fruit and vegetables in diet etc.) along with several environmental and geographic risk factors (barren land, radioactivity, heavy metals etc.) (11). Many dietary procarcinogens, especially nitrates, originate from salty foods (pickled vegetables, dried fish), processed meat and well water in rural areas (12,13). Dietary nitrates are reduced to nitrites by the flora of the mouth and stomach at a high pH and then react with amines and are converted to carcinogenic nitrosamines in the stomach. Approximately 20 % of salivary nitrate is reduced to nitrite by the oral flora, and this accounts for most (80%) of the gastric nitrite (14). Salivary nitrate and nitrite levels are positively correlated with the high prevalence of gastric cancers in endemic regions (11,15).

Several epidemiological and experimental studies have revealed the positive relationship between the consumption of salted, nitrated foods and the high incidence of esophageal and gastric cancers with the frequency of this cancer in high mountainous areas being correlated with the elevated nitrate concentration in home-smoked foods (13). In endemic upper GI cancer regions of China, nitrate, nitrite and nitrosamine levels have been found to be significantly high in pickled vegetables and regional drinking waters. The histopathological biopsy results of precancerous lesions of patients residing in these regions were also well correlated with the high nitrate levels in foods and regional drinking waters (12,16). Lipid peroxidation endproducts (malondialdehyde etc.) related to gastric carcinogens were also increased in gastric mucosal biopsies of rats fed with a salty diet (17). In addition, salty foods predispose to H.pylori colonization and premalignant gastric lesions (atrophic gastritis, intestinal metaplasia, dysplasia) (18).

In conclusion, the frequent consumption of traditional foods with carcinogenic potency (nitrate, nitrite, benzpyrene etc.) in the Van region of Eastern Anatolia, an endemic upper GI (esophageal and gastric) cancer region of Turkey on “the Asian cancer belt”, constitutes the most serious GI cance risk r in the context of a number of other ecological (environmental) risk factors.

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