Journal of BUON **15:** 89-93, 2010

ORIGINAL ARTICLE

Dietary factors and gastric cancer risk: hospital-based case control study

K. Lazarevic[1], A. Nagorni[2,3], N. Rancic[1], S. Milutinovic[1], L. Stosic[1], I. Ilijev[4]

[1]Public Health Institute Nis, [2]Gastroenterology and Hepatology Clinic, Clinical Center Nis, [3]School of Medicine, University of Nis, [4]Psychiatric Clinic, Clinical Center Nis, Nis, Serbia

Summary

Purpose: *To examine possible associations between dietary factors and gastric cancer risk among residents in the area of Nis, Serbia.*

Methods: *This hospital based case-control study was conducted at the Clinical Centre Nis between 2005 and 2006. Cases (n=102) with histologically confirmed gastric cancer and matched non-cancer patients (controls, n=204) were interviewed. Diet was assessed using a food frequency questionnaire and odds ratios (OR), 95% confidence interval (95% CI), and p-trends were calculated across tertiles of intake.*

Results: *High intake of salt, salty meals and hot food were associated with higher risk of gastric cancer. After searching for potential confounders, multivariate logistic regression analysis showed elevated risk for the highest vs. the lowest tertile of intake for smoked and barbecue meat (OR 4.21; 95% CI 1.43-12.37), processed meat (OR 9.17; 95% CI 2.78-15.23), desert (OR 2.85; 95% CI 1.28-6.38), potatoes (OR 4.79; 95% CI 1.44-5.94), pickled vegetables (OR 2.02; 95% CI 1.21-3.0) and milk (OR 5.08; 95% CI 1.59-10.16) intake but reduced for citrus fruits (OR= 0.13, 95% CI 0.03-0.53), other fruits (OR 0.05; 95% CI 0.02-0.18), allium vegetables (e.g. onion, garlic, leek) (OR 0.11; 95% CI 0.02-0.60) and cooked meat intake (OR 0.07; 95% CI 0.02-0.27). Intake of bread, dairy, fish, legumes and raw and cooked vegetables was not significantly related with gastric cancer risk.*

Conclusion: *A low risk diet for gastric cancer in the area of Nis should include increased fruits and alliums vegetables consumption and limited processed meat, salt, preserved food, deserts, potatoes and milk intake.*

Key words: dietary factors, gastric cancer

Introduction

Worldwide, gastric cancer is in the 4th place in incidence and it is the 2nd leading cause of death from cancer [1]. This relatively high death rate is due to the fact that gastric cancer is rarely diagnosed early. When detected, the disease is usually surgically unresectable [2]. This is the reason why the knowledge of risk factors for the development of gastric cancer is of utmost importance.

Risk for gastric cancer is related to an interaction between genetic and many different environmental factors. Changes in diet have been evoked to explain the large decrease in gastric cancer rate [3], although the role of specific foods or nutrients is still unclear [4]. Data shows that in Serbia mortality of gastric cancer in males is been moderately decreasing after 1990 [5].

The purpose of this study was to assess the relation between dietary factors and the risk of gastric cancer in Nis, Serbia.

Methods

This hospital-based case-control study was conducted between January 2005 and December 2006 in the Clinic of Surgery of the University Hospital in Nis (reference centre for South-East Serbia). Cases included 102 subjects with first-time histologically verified diagnosis of gastric adenocarcinoma. Age (±3 years), gender, and residence-matched controls were 204 subjects residing in the same geographical area and admitted to the same hospital as cases for acute, non-neoplastic conditions.

Correspondence to: Konstansa K. Lazarevic. Dr Milenka Hadzica 2/23, 18000 Nis, Serbia. E-mail: koni33@hotmail.com
Received 28-01-2009; Accepted 02-04-2009

Cases and controls were interviewed during their hospital stay by a physician. The structured questionnaire included personal information (name, gender, education) and lifestyle habits (smoking habits, dietary habits), personal medical history and family history of cancer. A food-frequency questionnaire (FFQ) was used to assess subjects' habitual diet, including information on weekly frequency of consumption of specific foods (98 items) in the course of 1 year prior to gastric cancer diagnosis or hospital admission (for controls). All cases and controls were recruited on a voluntary basis.

Statistical analysis

Univariate logistic regression analysis was performed to calculate the risk for gastric cancer for demographic and lifestyle habits. ORs and the corresponding 95% CI were computed by tertiles of daily food and group of food intake using multivariate logistic regression analysis. The lowest level of consumption (I tertile) was used as the reference category in the estimation. $p<0.05$ was considered statistically significant. All estimated ORs were adjusted for the impact of confounding variables (age, sex, residence, education, meals regularity, tobacco smoking, and history of cancer in first-degree relatives). Analyses were carried out by the SPSS version 10.1 software.

Results

Table 1 shows the distribution of gastric cancer cases and control subjects according to selected demographic variables.

Cases and controls were individually matched by age (±3 years), sex, and place of residence, with a case to control ratio of 1:2. All patients with gastric cancer were diagnosed after the fourth decade of life. Cases and controls had also similar age distribution, education level and marital status.

The prevalence of gastric cancer increased with higher prevalence of medical history of gastric diseases (OR 5.76; 95% CI 3.40-9.75; $p<0.01$) and family history of cancer in first-degree relatives (OR 2.44; 95% CI 1.41-4.24; $p<0.001$; Table 2).

Gastric cancer cases were more likely to be current smokers (OR 2.10; 95% CI 1.21-3.65; $p<0.001$). Among smokers, there was not any significant increase in risk with the number of cigarettes >20 per day. Duration of cigarette smoking (>20 years) increased the risk for gastric cancer (OR 2.80; 95% CI 1.18-4.27; $p<0.05$).

Irregular daily meals (only 1-2/day) increased the risk for gastric cancer (OR 3.38; 95% CI 1.92-5.98; $p<0.001$). We asked cases and controls if salt or hot spices and food was rarely or frequently added to their nutrition, and observed that frequent consumption of hot food

Table 1. Demographics of participants

Variable	*Cases (n)*	*Controls (n)*	*OR (95% CI)*	*p-value*
Gender				
Male	58	116		matched
Female	44	88		
Age (years)				
<50	3	7		
50-59	24	46		matched
60-69	37	74		
70-85	38	77		
Residence				
Rural	54	108		matched
Urban	48	96		
Education				
Primary or no school	59	101		
Secondary and high school	43	103	1.40 (0.84-2.33)	ns
Marital status				
Single	–	–		
Divorced or widowed	8	18		
Married	94	186	0.88 (0.34-2.24)	ns

ns: not statistically significant ($p>0.05$), OR: odds ratio, 95% CI: 95% confidence interval

(OR 6.82; 95% CI 3.54-13.23; p <0.001) and addition of salt to meals (OR 4.67; 95% CI 2.49-8.82; p <0.001) increased the risk for gastric cancer. We did not observe any significant association between coffee or hard liquor consumption and gastric cancer risk (Table 3).

Multivariate logistic regression analysis (Table 4) showed that risk for smoked and barbecue meat (OR the highest vs. the lowest tertile = 4.21; 95% CI 1.43-12.37; p <0.01), processed meat (OR 9.17; 95% CI 2.78-15.23; p <0.001), milk (OR 5.08; 95% CI 1.59-10.16; p <0.01), sugar and desert (OR 2.85; 95% CI 1.28-6.38; p <0.05), potatoes (OR 4.79; 95% CI 1.44-5.94; p <0.05) and pickled vegetables (OR 2.02; 95% CI 1.21-3.0; p <0.05) was positively related to gastric cancer.

An inverse relationship was found for citrus fruits (OR 0.13; 95% CI 0.03-0.53; p <0.01), other fruits (OR 0.05; 95% CI 0.02-0.18; p <0.01) and allium vegetables (OR 0.11; 95% CI 0.02-0.60; p <0.001) consumption as well as for cooked meat consumption (OR 0.07; 95% CI 0.02-0.27; p <0.001).

Intake of bread, milk, dairy, fish, legumes and raw and cooked vegetables were not significantly related with gastric cancer risk.

Discussion

In the present study, we have investigated the influence of dietary factors with regard to the risk for gastric cancer. Since gastric cancer development is also associated with lifestyle and sociodemographic factors, these were also analysed in multivariate logistic regression models.

Consistent with previous studies, dietary habits such as irregular meals, hot and spicy food consumption were identified as risk factors for gastric cancer [4]. Irregular meals lead to hyperinsulinemia and increased insulin-like growth factor (IGF) bioavailability. Previous studies indicate that IGF is a promoter of the process of gastric carcinogenesis [6-8]. This indicates a link between hyperinsulinemia and gastric cancer. Hot foods can irritate and erode the gastric mucosa.

We confirmed also the significance of the most of previously established dietary risk factors for gastric cancer [4]. Fruit (both citrus and non-citrus) consumption has a favorable effect on the prevention of gastric cancer. The inverse relationship between fruits consumption and gastric cancer risk may be explained

Table 2. Medical history and risk of gastric cancer according to univariate regression analysis

Variable	*Cases (n)*	*Controls (n)*	*OR (95% CI)*	*p-value*
Previous medical history				
Past history of gastric disease	58	38	5.76 (3.40-9.75)	<0.001
Use of aspirin	30	69	0.82 (0.47-1.41)	ns
Family history				
Gastric cancer	–	–	–	–
History of cancer in 1st degree relatives	41	44	2.44 (1.41-4.24)	<0.001

For abbreviations see footnote of Table 1

Table 3. Lifestyle habits and risk for gastric cancer according to univariate regression analysis

Variable	*Cases (n)*	*Controls (n)*	*OR (95% CI)*	*p-value*
Tobacco smoking				
Current smoker	38	45	2.10 (1.21-3.65)	<0.001
Number of cigarettes >20/day	26	27	1.44 (0.53-3.96)	ns
Duration >20 years	27	21	2.80 (1.18-4.27)	<0.05
Dietary habits				
Irregular meals (1-2/day)	39	17	3.38 (1.92-5.98)	<0.001
Frequent addition of salt to meals	38	23	4.67 (2.49-8.82)	<0.001
Frequent consumption of hot foods	42	19	6.82 (3.54-13.23)	<0.001
Hard liquor consumption (≤ 100 ml/day)	19	27	2.07 (0.98-4.40)	ns
Coffee consumption (cups of coffee ≥ 4 daily)	38	61	1.11 (0.62-1.98)	ns

For abbreviations see footnote of Table 1

Table 4. Amount of food intake related to gastric cancer according to multivariate logistic regression analysis*

Food or food group	*II tertile OR (CI 95%)*	*III tertile OR (CI 95%)*	*p-value*
Bread	1.43 (0.42-2.89)	1.61 (0.60-4.33)	ns
Cooked meat	0.30 (0.11-0.80)	0.07 (0.02-0.27)	<0.001
Smoked and barbecued meat	1.58 (0.54-4.61)	4.21 (1.43-12.37)	<0.01
Processed meat	4.37 (1.37-13.90)	9.17 (2.78-15.23)	<0.001
Fish	0.18 (0.05-0.57)	0.21 (0.02-2.02)	ns
Milk	2.60 (0.86-7.87)	5.08 (1.59-10.16)	<0.01
Dairy	0.42 (0.20-1.23)	0.63 (0.33-1.72)	ns
Sugar and deserts	2.58 (0.69-9.58)	2.85 (1.28-6.38)	<0.05
Potatoes	1.14(0.26-4.97)	4.79 (1.44-5.94)	<0.05
Pulses	0.54 (0.27-1.09)	0.96 (0.37-2.54)	ns
Allium vegetables	0.25 (0.06-1.07)	0.11 (0.02-0.60)	<0.001
Cooked vegetables	0.15(0.04-0.53)	0.44 (0.33-6.34)	ns
Raw vegetables	0.11 (0.02-0.66)	0.17 (0.01-2.64)	ns
Pickled vegetables	1.26 (0.28-5.62)	2.02 (1.21-3.0)	<0.05
Citrus fruit	0.62 (0.24-1.60)	0.13 (0.03-0.53)	<0.01
Other fruit	0.03 (0.01-0.17)	0.05 (0.02-0.18)	<0.001

*Estimates from multivariate logistic regression analysis including terms for age, sex, residence, education, meals regularity, tobacco smoking, and history of cancer in the first degree relatives.
ns: not statistically significant ($p>0.05$)

through the action of antioxidants (such as vitamin C), carotenoids, flavonoids, phytosterols and d-limonene (from citrus fruits). They protect gastric mucosa from oxidative stress associated with high salt consumption and nitrate and nitrite intake from food. Nitrites and salt are found mainly in processed meats, smoked meats, pickled and salty preserved vegetables. Evidence from this and other epidemiologic studies suggests that intake of salty preserved vegetables, processed meat and smoked meat increased the risk for gastric carcinogenesis [4].

However, the increased risk of gastric cancer associated with high consumption of meat may be related not only to methods of preservation but also to cooking methods. The risk of gastric cancer has been related to the intake of heterocyclic amines and polycyclic aromatic hydrocarbons, generated by cooking meat or fish at high temperatures [9,10]. We were unable to confirm any potential association between fish intake and gastric cancer. Fish consumption in Serbia is relatively infrequent [11], and in our study the number of subjects who consumed fish was relatively small.

According to the World Cancer Research Fund [4], vegetables, particularly green vegetables and legumes intake, are probably associated with reduction of gastric cancer. In the present study, no inverse relationship was observed both for raw and cooked vegetables, as well as for legumes. One possible explanation of these results is that fresh vegetables and pulses consumption in our national diet is high. As with other published data, we found that alliums vegetables consumption decreased the risk for gastric cancer.

While potatoes are classified as vegetables, they are also grouped separately from non-starchy vegetables. In our investigation, the significant increase in the risk of gastric cancer associated with high potatoes consumption was unexpected. Most [12-15], but not all case-control studies [16] did not report a significant association between potatoes consumption and gastric cancer risk. It is important to note that across the world people consume various forms of potatoes (yam, sweet potato and cassava) and this fact must be taken into account when interpreting the findings from various studies. Potatoes contain vitamin C, for example, and the orange varieties of sweet potatoes contain carotenoids. Starch content varies from around 15-20% in sweet potatoes to 25-30% in yams. Cooking sweet potatoes converts as much as 75% of the starch into maltose.

The mechanism by which a high consumption of starch may increase the risk of gastric cancer is unclear. Several possibilities have been suggested including physical irritation of gastric mucosa and reduction in gastric mucin and insulin/ gastric cancer hypothesis [6-8].

In the present study, however, intake of breads (starchy-foods) was not associated with increased risk. The results of case-control studies also do not support an increase in gastric cancer risk with higher sugar and desert intake [4]. In the present study, a high intake of sugar and desert may indicate a diet low in fruits which has

been consistently shown to increase gastric cancer risk. Our data further suggests that, as most of other published data [13,17], consumption of milk can be classified as a risk factor for gastric cancer. It remains unknown which compounds in milk may be responsible for gastric carcinogenesis. The observed positive association of milk consumption and gastric cancer risk may be a consequence of a previous gastric disease and the consequent consumption of milk to relieve gastric pain.

The present study confirms a protective role of fruits and alliums vegetables on gastric carcinogenesis, and supports the hypothesis of an increased risk with a more frequent consumption of processed meat, and perhaps salt intake. From our data, we can conclude also that increased intake of milk, potatoes, sugar and desert are associated with higher gastric cancer risk in the area of Nis.

References

1. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin 2005; 55: 74-108.
2. Maconi G, Manes G, Porro GB. Role of symptoms in diagnosis and outcome of gastric cancer. World J Gastroenterol 2008; 14: 1149-1155.
3. Roder DM. The epidemiology of gastric cancer. Gastric Cancer 2002; 5 (Suppl 1): 5-11.
4. World Cancer Research Fund/American Institute for Cancer Research. Food, nutrition, physical activity and the prevention of cancer: a global perspective. Washington DC: AICR, 2007.
5. Markovic Denic L, Zivkovic S, Sipetic S, Vlajinac H, Kocev N, Marinkovic J. Time trends in cancer mortality in central Serbia. Soz praventivmed 2006; 51: 211-218.
6. Zhang ZW, Newcomb PV, Moorghen M et al. Insulin-like growth factor binding protein-3: relationship to the development of gastric pre-malignancy and gastric adenocarcinoma (United Kingdom). Cancer Causes Control 2004; 15: 211-218.
7. Franciosi CM, Piacentini MG, Conti M et al. IGF-1 and IGF-1BP3 in gastric adenocarcinoma. Preliminary study. Hepatogastroenterology 2003; 50: 297-300.
8. Zhao MD, Hu XM, Sun DJ, Zhang Q, Zhang YH, Meng W. Expression of some tumor-associated factors in human carcinogenesis and development of gastric carcinoma. World J Gastroenterol 2005; 11: 3217-3221.
9. Sugimura T, Wakabayashi K, Nakagama H, Nagao M. Heterocyclic amines: Mutagens/carcinogens produced during cooking of meat and fish. Cancer Sci 2004; 95: 290-299.
10. De Stefani E, Boffetta P, Mendilaharsu M, Carzoglio J, Deneo-Pellegrini H. Dietary nitrosamines, heterocyclic amines, and risk of gastric cancer: a case-control study in Uruguay. Nutr Cancer 1998; 30: 158-162.
11. Serbian Republic Statistic Office, Report on household budget survey, 2000-2005.
12. WCRF/AICR. Food, nutrition and the prevention of cancer: a global perspective. World Cancer Research Fund in Association with American Institute for Cancer Research. Washington DC: WCRF/AICR, 1997.
13. Sipetic S, Tomic-Kundakovic S, Vlajinac H, Jankovic S, Marinkovic J, Maksimovic J. Diet and gastric cancer. Vojnosanit Pregl 2003; 60: 697-705 (in Serbo-Croatian with Engl. abstr).
14. Ngoan LT, Mizoue T, Fujino Y, Tokui N, Yoshimura T. Dietary factors and stomach cancer mortality. Br J Cancer 2002; 87: 37-42.
15. Jansen MC, Bueno-deMesquita HB, Rasanen L et al. Consumption of plant foods and stomach cancer mortality in the seven countries study. Is grain consumption a risk factor? Seven Countries Study Research Group. Nutr Cancer 1999; 34: 49-55.
16. De Stefani E, Correa P, Boffetta P, Deneo Pellegrini H, Ronco AL, Mendilaharsu M. Dietary patterns and risk of gastric cancer: a case-control study in Uruguay. Gastric Cancer 2004; 7: 211-220.
17. Munoz N, Plummer M, Vivas J et al. A case-control study of gastric cancer in Venezuela. Int J Cancer 2001; 93: 417-423.