RESEARCH COMMUNICATION

Salt Taste Preference, Sodium Intake and Gastric Cancer in China

Zhiyong Zhang, Xiefu Zhang*

Abstract

Aim: The risk factors mostly strongly associated with gastric cancer are gastric bacteria *Helicobacter pylori* and diet. By using a case-control study among residents in China, we examined the association between sodium intake, presence of H,pylori, and gastric cancer risk. Methods: A population-based case-control study including 235 cases and 410 controls were used. Potential risk factors of gastric cancer were interview for cases and controls by questionnaire, salt taste preference was measured for all subjects, and IgG antibodies to H,pylori was used for H.pylori infection. Risk measures were calculated using unconditional logistic regression. Results: H.pylori infection and smoking increased the risk of gastric cancer, with the OR(95%CI) of 1.91(1.32-2.79) and 1.47(1.05-2.05), respectively. Dietary sodium intake independently increased the risk of gastric cancer. Participants with the highest sodium intake(>5g/day) had a high gastric cancer risk [OR(95%CI)= 3.78(1.74-5.44)]. Participants with the salt taste preference at 7.3g/L and ≥14.6g/L showed higher risk of gastric cancer [OR(95%) for 7.3g/L and ≥14.6g/L were 5.36(2.72-10.97) and 4.75(2.43-8.85), respectively]. A significantly interaction was found between salt taste preference and H.pylori infection (p=0.037). Salt taste preference was significantly correlated with sodium intake (Correlation coefficient=0.46, p<0.001). Conclusion: Salt taste preference test could be a simple way to evaluate an inherited characteristic of sodium intake, and our study confirms the gastric cancer is associated with sodium intake and H.pylori.

Keywords: Gastric cancer - salt taste preference - sodium intake - *H.pylori*

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Introduction

Gastric cancer is the second most frequent cause of deaths from cancer and fourth most common cancer in the world, with estimated 650000 deaths and 880000 new cases per year, almost two-thirds of which occurred in developing countries. In China, gastric cancer the the thrid cuase of dealth from the most common cancer, with an age-standardized incidence of 37.1 and 17.4 cases per 100, 000 person-years for men and women, respectively, according to the 2005 national cancer statistics (Yang, 2006). Therefore, prevention of gastric cancer is one of the most important cancer control strategy both in China and around the world.

Geographic and ethnic difference, trend in cancer incidence with time, and changes in incidence patterns observed among immigrants indicate that gastric cancer is closely associated with modifiable factors, such as diet. Subtantial evidence from ecological, case-control, and cohort studies strongly suggest that the risk of cancer could increase with a high intake of some traditional salt-preserved food and high sodium intake, and that the risk could be decreased with a high intake of fruits and vegetables (WCRF/AICR, 2006; WCRF/AICR, 2007). Other established non-dietary factors include cigarette smoking and infection with the bacterium, Helicobacter pylori (Loh ,2007).

In experimental studies, with rats, ingestion of salt is known to cause gastritis, and when coadministered, enhance the carcinogenic effect of known gastric carcinogens, such as N-methyl-N-nitro-N-nitrosoguanidine (Fox et al., 1999; Kato et al., 2006). A high intragastric salt concentration destrogys the mucosal barrier, and leads to inflammation and damage such as diffuse erosion and egeneration. The induced proliferous change might enhance the effect of food-derived carcinogens. Lots of epidemiologic studies study on the relationship between salted food and gastric cancer, but the results is conflicting (WCRF/AICR, 2006; WCRF/AICR, 2007). Previous studies which evaluate the salt preference are mainly determined by the subjective feeling of selected cases, few studies use objective way to assess the salt preference. Salt taste preference is the capacity to identify the flavor of salt, and can influence salt appetite and sodium intake (Nilsson, 1979). Our study aimed to analyze relationship between salt taste preference and gastric cancer, and confirmed whether salt taste preference could reflect the sodium intake. We are not aware of any previous study examining such relationship.

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Materials and Methods

A population-based case-control study was carried out in the the Department of Surgery of Zhengzhou University, and Urumchi Friendship Hospital. Cases in the study included 235 patients aged 40-75 years histological confirmed diagnoses with gastric cancer January 2007 to December 2010. Potential controls were identified from health individuals visiting Hospital for routine physical examination. Totally, we had 410 controls that were malignant tumors or digestive tract disorders free. The controls ranged from 35-77 years old.

Questionnaire is consisted of a detailed food frequency section, and questions on education, smoking history, alcohol intake and dietary sodium intake. The reliability and validity of this questionnaire were assessed in the pilot study. Face to face interview was performed for all subjects. Two interviewers were trained and were not aware of the study hypothesis. Cancer patients were asked to their usual diet during the year prior to diagnosis. Controls were asked about their usual diet during the year before interview. For each subject, daily sodium intake in grams was computed for each food item and food group, with the food group intake computed by adding up the amounts of each single item or group consumed per day.

After interviewing for questionnaires, the salt preference was assessed by carrying out by dropping several NaCl solutions on the tip of the tongue. Three drops of the test solution were placed on the tongue. After 10 s closing the mouth, the cases and controls mentioned which taste of usually food was perceived. The solutions were offered in increasing concentrations. Between the tests, the mouth was washed by distilled water, with one minute intervals among successive tests. The concentrations of each test NaCl solution were classified into ten grades from 0.45 g/L to 14.6 g/L with 0.9g/L interval, and the recognized NaCl solution for normal individuals was usually 0.9g/L.

Questions on food intake considered the usually food recipe in China, a total of 65 food items/groups or beverage categories were validated. Diet preference was classified into two categories: <3 times/ week and ≥3 times/week. Cigarette smokers were divided into non-smokers and smokers who smoked more than 10 cigarettes per week for at least 6 months; Alcohol drinkers were classified into non-drinkers and drinkers who consumed more than 50 mL of distilled spirits per week for at least 6 months. Sodium intake was estimated by considering the food's intrinsic sodium content plus an estimated of added salt during cooking, taking into account the specific contribution of the different food items/groups. The sodium intake were categorized into <3g/day, 3-5g/day and >5g/day.

A blood sample was drawn and serum was kept frozen at -20°C. A H. pylori serum IgG titres were quantified by ELISA. Participants were classified as negative if they had <16RU ml-1, as borderline if their antibody concentration was between 16 and 22 RU ml-1 and as positive if this was ≥22 RU ml-1, according to the manufacturer's instructions. In our analysis, subjects with borderline IgG titres were classified as infected.

The ethnics of committee of Zhengzhou University and Urumchi Friendship Hospital reviewed and approved the study, and informed consent was obtained from all participants.

Table 1. Crude Odds Ratios and 95% CIs for Lifestyle and Dietary Factors and Gastric Cancer

Characteristic	Cases N=235	Controls N=410	OR (95% CI)	P value
Age (yr)	53.3±6.7	52.8±5.9	-	0.16
Male	166(70.6)	258(62.9)	1.42 (1.00-2.04)	0.047
Literate	99(42.1)	189(46.1)	0.85 (0.61-1.19)	0.33
Smoking	128(54.5)	184(45.8)	1.47 (1.05-2.05)	0.02
Drinking	53(22.6)	80(19.5)	1.20 (0.79-1.81)	0.36
H.pylori infection				
Positive	177(75.3)	252(61.5)	1.91 (1.32-2.79)	0.0003

Data are n (%); OR, Crude Odds ratio

Table 2. Adjusted Odds Rations and 95% CIs for Sodium Intake and Salt Taste Preference

	Cases(%) N=235	Controls(%) N=410	OR (95% CI)	P value
Sodium intake (g/day)				
Mean	3.92±0.17	3.15±0.14	-	-
<3g/day	54(23.0)	115(28.1)	Reference	
3-5g/day	111(47.2)	213(51.9)	1.95 (1.23-3.03)	0.012
>5g/day	70(29.8)	82(20.0)	3.78 (1.74-5.44)	0.012
Salt taste preference(g/L)				
≤0.45	10(4.3)	41(10.0)	0.82 (0.29-2.07)	
0.9	21(8.9)	74(18.1)	Reference	
1.8	35(14.9)	119(29.0)	1.12 (0.61-2.26)	
3.6	51(21.7)	86(20.9)	2.37 (1.27-4.63)	
7.3	61(25.9)	41(10.0)	5.36 (2.72-11.0)	
≥14.6	57(24.3)	49(12.0)	4.75 (2.43-8.85)	

OR adjusted for sex, age, education level, smoking, drinking and *H.pylori* infection.

Statistical analysis

The unconditional logistic regression was used to calculate odds ratios (OR), and corresponding 95% confidence intervals (CI) for gastric cancer in relation to exposure of interest. The association between salt consumption and gastric cancer was quantified using crude and gender-, age-, education-, smoking- and H.pylori infection-adjusted odds ratios (ORs) and the corresponding 95% confidence intervals (95% CIs) were computed by unconditional logistic regression. Stratified analyses of salt food intake were performed according to H.pylori infection All reported trend test significance levels (p-values) were two-sided (Woodward, 1999). The coherence of salt taste preference with sodium intake was detected by spearman correlation analysis. The significant level was set at 5%. All the calculations were performed with the STATA 9 software program.

Results

Most cancers were located in the non-cardia region (206 non-cardia gastric cancer, accounted for 87.7%). The general variables and proportion of selected risk factors among cases and controls was shown in Table 1. Of 235 cases and 410 controls, 166 (71%) of the cases and 258 (63%) of the controls were males. The average age of cases

and controls were 53.3 and 52.2 years, respectively. The prevalence of H.pylori infection was 75.3% in cases and 61.5% in controls, and the OR(95%) of H.pylori infection for gastric cancer was 1.91(1.32-2.79). The proportion of literate was 42.1% in cases, which was lower than that in controls. The proportions of smoking and drinking in cases were higher than those in controls. The smoking was significantly association with gastric cancer with the OR(95%) of 1.47 (1.05-2.05).

The median sodium intake from questionnaires was higher for cases than controls (3.92±0.17g/day vs 3.15±0.14g/day), as well as the salt taste preference in cases was higher than controls. Participants with the highest sodium intake (>5g/day) had a high gastric cancer risk [OR(95%CI)= 3.78(1.74-5.44)]. Comparison with the normal salt taste preference of 0.9g/L, participants with the salt taste preference at 3.6g/L or above showed higher risk of gastric cancer (Table 2). Especially for salt taste preference at 7.3g/L and ≥14.6g/L, a heavy risk of gastric cancer was found.

The mechanism of sodium intake for gastric cancer risk may be through its interaction with *H.pylori,* therefore, we further performed stratified analysis by *H.pylori* infection status. The stratified analysis indicated salt tasted preference had lower gastric cancer in participants with negative H.pylori infection compared with those with positive H.pylori infection [salt taste preference at 0.9-3.6g/L: OR(95%CI)=1.42(0.73-3.56) for negative H.pylori infection and 2.64(1.35-4.98) for positive H.pylori infection; salt taste preference above 3.6 g/L: OR(95%CI)= 3.77(1.75-8.21) for negative H.pylori infection and 5.74(2.71-10.62) for positive H.pylori infection]. Significantly interaction was observed between *H.pylori* infection and salt taste preference (p=0.037).

We further analyzed the association between salt taste preference and sodium intake, and a moderate correlation was observed between them (correlation coefficient=0.46). It proved the salt taste preference could represent the sodium intake and reflect the sodium intake habit.

Discussion

The present population based case-control study has demonstrated that the dietary sodium intake independently increased the risk of gastric cancer, regardless of the H.pylori infection, smoking and other risk factors of gastric cancer. Most observational studies have used questionnaires to assess risk of dietary sodium intake for gastric cancer, and the estimated OR was ranged from 0.53 to 24.92 (Tsugane, 2005; Wang et al., 2009). In our study, subjects with high sodium intake were approximately 3.78 times risk as high as those with the low sodium intake. Subjects with salt taste preference at 7.3g/L and above were observed heavy risk of gastric cancer, and it is a simple and better way to reflect the sodium intake.

In our study, high sodium intake is independently associated with gastric cancer risk. The increased risk from high sodium intake in gastric cancer might be because of compounds other than salt that are produced during the preservation process. High salted food, such as processed meat, pickled vegetable or dried fish, whose consumption is used as a surrogate for salt exposure, also have a high content of nitrosated compounds. Ingestion of those high salted food could induce gastritis and coadministrate with N-methyl-N-nitro-N-nitrosoguanidine to enhance the carcinogenic effect of gastric carcinogens (Tatamatsu et al., 1975; Takahashi and Hasegawa, 1985). In our study, the salt taste preference is proved to be associated with sodium intake, and is observed an increased risk of gastric cancer, supporting the role of salt and nitrosated compounds in gastric carcinogenesis.

The proposed mechanisms which salt can cause gastric cancer are either direct damage to the gastric mucosa leading to hyperplasia of the gastric pit epithelium with increased potential for mutations or effect of interaction with H.pylori, as the damage caused by salt may also increase gastric H.pylori colonization (Fox et al., 1999; Nozaki et al., 2002). This suggests there may be interaction between sodium intake and H.pylori infection, and this was confirmed in our study. Other major potential confounders did not change the deleterious effect of high sodium intake for gastric cancer, such as smoking, drinking, gender and age (data not shown). This implies the high sodium intake is independently associated with gastric cancer.

A major problem in assessing sodium intake from questionnaire is that people usually ignore or unable to report accurately their dietary in the past. Excretion of sodium in urine over a 24-h period could accurately reflect the sodium ingested from different sources (Montes et al., 1985; Tsugane et al., 1992), but it is impracticable for a large-scale population study. The result of 24h urinary is not optimal to be used in case-control study because it could only reflect the sodium intake in the past 24 hours. However, patients usually change their sodium intake habit after diagnosis. Salt taste preference is a personal characteristic of individuals' and may be eventually be a practical way to evaluate who eats more salt(Nilsson, 1985), and who has the higher preference for salt. Salt taste preference test has been used for detecting hypertension in studies (Weinberger et al., 1986; Campese, 1994), and it indicated that hypertensive individuals were significantly more salt sensitive than the normotensive individuals(Weinberger, 1996). Our study proved that the subject who has high salt taste preference was observed to have high sodium intake (Table 4). This consistency of salt taste preference and sodium intake indicated this test is a better way to reflect the salt taste preference and sodium intake. Also, salt taste preference test is simpler, cheaper and more acceptable than the 24h urinary test, and patients could easily identify the taste before diagnosis.

There are variation methods for measuring sodium intake previously, and most studies used the frequency of salt consumption levels and self-reported sodium intake from questionnaires. The frequency of salt consumption levels could not accurately reflect the past sodium intake habits, because subjects with high frequency of salt consumption could take little salt each time. The sodium intake calculated from questionnaire may be associated with recall bias. Cases may over-report their exposures perceived as causal(Botterweck et al., 1998). Therefore, these methods may induce measurement bias

and recall bias. However, Salt taste preference test is related to sodium intake and consumption, it is an indirect objective way to reflect the salt preference and avoid the measurement bias.

Our study indicated that the importance of diet, especially intake of sodium intake, play a role in the etiology of gastric cancer. The risk of sodium intake is varied by the *H.pylori* status of the individual. Salt taste preference could reflect the characteristic of sodium intake, and our study confirms its association with the sodium intake and gastric cancer. The role of salt taste preference test could be further studied to answer the questions raised from the present study.

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