RESEARCH COMMUNICATION

Evaluation of Non-viral Risk Factors for Nasopharyngeal Carcinoma in Thailand: Results from a Case-control Study

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Abstract

Nasopharyngeal cancer (NPC) is rare in most populations but common in Southern China and Southeast Asia. To understand the role of environmental exposures on risk of NPC, a case-control study was conducted among 327 newly diagnosed case of NPC and 327 controls matched to case on sex, age and geographic residence. Information was collected by interviewer about demographic variables, cigarette smoking, alcohol drinking, eating habits, past history of disease, family history of cancer and a lifetime history of every job that was held for one year or longer. The result indicates that cigarette smoking was associated with an increased risk of NPC (OR= 2.41, 95% CI 1.61-3.6). There was indication of increased risk with a history chronic ear or nose disease (OR= 2.71, 95% CI 1.45-5.06). Occupational exposure to wood dust was also associated with a higher risk (OR= 1.63 95% CI 1.02-2.61). Furthermore, lower education was found to be positively associated with NPC (OR= 2.71, 95% CI 1.45-5.06). There was no association between NPC and salted fish intake (OR= 1.38, 95% CI 0.84-2.25) or alcohol consumption (OR= 0.88, 95% CI 0.58-1.33). Our results suggest that cigarette smoking, past history of ear or nose disease and occupational exposure to wood dust may play a role in the development of NPC in the Thai population.

Keywords: NPC - case-control study - risk factors - smoking - wood dust - ear & nose disease - Thailand

Asian Pacific J Cancer Prev, **11**, 929-932

Introduction

The incidence of nasopharyngeal carcinoma (NPC) varies widely according to geographic location and ethnic background. Over the year, numerous studies have shown that the etiology of NPC is multifunctional, including genetic, environmental, and virological factors. Among these factors, EBV seems to be the strong association between infection of EBV and NPC (International Agency for Research on Cancer, 1997). However, given the universality of EBV infection but the unique geographic distribution of NPC, factors other than EBV are also believed to be important determinants of the risk for NPC.

Numerous factors have been postulated to be linked to the development of NPC, including consumption of salted and processed foods, occupational exposure to formaldehyde and dusts, and cigarette smoking (Hildesheim and Levine, 1993). Most studies of NPC have been conducted in China or among individuals of Chinese ethnicity. In Thailand, the age-standardized incidence of NPC during the period 2001-2003 was 3.7/100,000 among male and 1.2/100,000 among females (Khuhaprema et al., 2010), rates which are intermediate between in China and in Western Countries (Burt et al., 1992; Jia et al., 2006).

Little is known about risk factors for NPC in this population. We therefore conducted a case-control study on NPC in Thailand, the aim being to investigate factors which increase the risk of NPC.

Materials and Methods

Study Population

Cases were all new incident NPC cancer patients histologically diagnosed at the National Cancer Institute in Bangkok and at regional cancer centers during the period of 2007- 2008. Controls were randomly selected from healthy person who visited patients admitted to the same center, matched to case for sex, age (±5 years) and residence area. In total, 327 pairs of case-control were recruited in the study period.

The study was approved by the ethical review committee for research in human subjects, National Cancer Institute, Thailand.

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Data Collection

Face to face interviews were done by trained nurse interviewers. Same questionnaires were used for both case and controls. Information was collected about demographic variables, tobacco smoking, alcohol intake, eating habits, past history of disease, family history of NPC in first degree relatives and a life time history of job that was held for one year and longer. The list of occupations reported by subjects was reviewed by an industrial hygienist. A list of occupations classified as likely to involve exposure to wood dust is provided in Table 1. Blood test for EBV latent infection was done using IgA antibodies for viral capsid antigen (IgA VCA), tests were done by indirect immunofluorescence method. Cut point for positive result at titer 1:10. For cases, diagnoses date and pathological results were collected from treatment documents.

Data Analysis

Statistical significance of differences between cases and controls characteristics were assessed by chi-square test, except for religion and family histories of NPC were assessed by Fisher's exact test, and mean age difference of the two groups was assessed by t-test. Association between risk factors and NPC were assessed by bivariate logistic regression for crude odds ratio (OR) and conditional logistic regression for OR adjusted for smoking and education. 95 % confidence intervals (95 % CI) were used for determine statistical significant. In this study, EBV infection was not adjusted for potential confounder since EBV is considered to be a necessary risk factor for the development of NPC and >90% of our NPC cases were seropositive for IgA-VCA antibodies.

Results

Table 2 shows the main characteristics of case and controls of 327 cases, 242 (74%) were males, and 85(26%) were females. The mean age of patients (48.3 years) was similar to controls (47.9 years). Race, religion and marital status were not different between case and controls. However, case showed lower education than controls. Most of case 296/327(90.5%) were infected to EBV but only 27.5 % (90/327) of controls were seropositive for IgA-VCA. According to WHO classification, for all 327 cases, 237 cases (72.5%) were identified as undifferentiated cell type, 79 cases (24.2%) were non-keratinizing cell type and 5 cases (1.5%) were squamous cell type.

Cigarette smoking was associated with a significantly increase risk of NPC (OR= 2.41, 95% CI 1.61-3.6)(Table 3). There was no association between alcohol consumption and NPC risk (OR= 0.88, 95% CI 0.58-1.33). Education was inversely associated with disease. Participants reporting less than high school education had a OR= 2.6 (95% CI 1.66-4.11) compared with those with more than high school education.

Consumption of salted fish was more frequent for case than for control, but the difference was not statistically significant (OR= 1.38, 95% CI 0.84-2.25). Our case showed a significantly higher likelihood of having a history of chronic ear or nose condition (OR= 2.71, 95% CI 1.45-5.06). After adjustment for cigarettes smoking and education, the association was observed between wood dust exposure and NPC (OR= 1.63, 95% CI 1.02-2.61).

Table 1. Wood Dust Exposure Occupations

Occupations	All subjects	Cases	Controls
Carpenters	24	14	10
Construction workers	20	12	8
Cabinetmakers	14	10	4
Sawyers/plywood makers / related wood-processing workers	12	6	6
Plasterers	8	6	2
Field crop farmers	4	2	2
General farmers	4	4	-
Forestry workers	3	1	2
Laborers	3	2	1
General managers	2	1	1
Retail trade salesmen	2	1	1
Construction supervisors	2	2	-
Charcoal workers	2	2	-
Painters	2	-	2
Computer programmers	1	-	1
Stock clerks	1	-	1
Prison guards	1	1	-
Groundsmen	1	-	1
Paper product supervisors	1	-	1
Welder and flame-cutters	1	-	1

Discussion

We conducted a case-control study of NPC in Thailand, an intermediate-risk population for this malignancy. Results from the present study indicate that cigarette smoking is associated with risk of NPC. An etiological link between cigarette smoking and NPC risk is biologically plausible since the nasopharynx is a site directly exposed to smoke during cigarette smoking. Tobacco smoke is a complex mixture of over 4,000 compounds; > 60 of

Table 1. General Characteristics of the Study Population

Characteristics		Cases (327)	Controls (327)	p-value
Age	Mean ± S.D.	48.3±12.7	47.9±12.5	0.67
Gender	Male	242 (74.0)	242 (74.0)	1.00
	Female	85 (26.0)	85 (26.0)	
Race	Thai	309 (94.5)	315 (96.3)	0.26
	Chinese/Thai	18 (5.51)	12 (3.67)	
Religion	Buddhist	324 (99.1)	323 (98.8)	1.00
	Others	3 (0.92)	4 (1.22)	
Marital status	Single	43 (13.2)	47 (14.4)	0.46
	Married	253 (77.4)	255 (78.0)	
Education	≤ 12 years	283 (86.5)	230 (70.3)	< 0.001
	> 12 years	44 (13.5)	97 (29.7)	
EBV infection	No	23 (7.03)	225 (68.8)	< 0.001
	Yes	296 (90.5)	90 (27.5)	
Cell type				
Undifferentiated		237 (72.5)	-	
Non-keratinizing		79 (24.2)	-	
Squamous cell		5 (1.53)	-	
Epithelial, NOS		6 (1.83)	-	

P-values were calculated by chi-square test; except age was calculated by t-test and religion was calculated by Fisher's exact test. NOS, not otherwise specified

Table 1. General Characteristics of the Study Population

Characteristics		Cases (327)	Controls (327)	Crude OR (95 % CI)	Adjusted OR (95 % CI)
Tobacco smoking	No	121 (37.0)	180 (55.1)	1	1
	Yes	206 (63.0)	147 (45.0)	2.09 (1.53 – 2.85)	2.41 (1.61 – 3.60)
Alcohol intake	No	129 (39.5)	146 (44.7)	1	1
	Yes	198 (60.6)	181 (55.4)	1.24 (0.91 – 1.69)	0.88 (0.58 – 1.33)
Salted fish consumption	< 1 time/week	270 (82.6)	284 (86.9)	1	1
	≥ 1 time/week	57 (17.4)	43 (13.2)	1.39 (0.91 – 2.14)	1.38 (0.84 – 2.25)
Fermented fish consumption	< 1 time/week	178 (54.4)	193 (59.0)	1	1
	≥1 time/week	149 (45.6)	134 (41.0)	1.21 (0.89 – 1.64)	1.18 (0.71 – 1.96)
Educational level	> 12 years	44 (13.5)	97 (29.7)	1	1
	≤ 12 years	283 (86.5)	230 (70.3)	2.71 (1.83 – 4.03)	2.62 (1.66 – 4.11)
Wood dust exposure	Unexposed	265 (81.0)	290 (88.7)	1	1
	Ever exposed	62 (19.0)	37 (11.3)	1.83 (1.18 – 2.84)	1.63 (1.02 – 2.61)
Family history of NPC	No	322 (98.5)	325 (99.4)	1	1
	Yes	5 (1.53)	2 (0.61)	2.52 (0.49 – 13.10)	2.32 (0.42 – 12.71)
History of disease*	No	284 (86.9)	310 (94.8)	1	1
	Yes	43 (13.2)	17 (5.20)	2.76 (1.54 – 4.95)	2.71 (1.45 – 5.06)

*chronic ear/nose

the compounds are carcinogens (International Agency for Research on Cancer, 2004). Several studies in other high and low risk areas have also observed a positive association between cigarette smoking and NPC (Yu et al., 1990; Nam et al, 1992; Chow et al., 1993; West et al, 1993; Friborg et al., 2007) although some studies failed to detect such an association (Ning et al., 1990; Sriamporn et al., 1992; Lee et al., 1994; Zheng et al., 1994)

In the present study, we did not observe an increased risk of NPC association with alcohol consumption. Our finding is consistent with those from most previous studies (Henderson et al., 1976; Geser et al., 1978; Chen et al., 1990; Ning et al., 1990; Sriamporn et al., 1992). It is believed that the nonviral exposure most consistently and strongly associated with the risk of NPC is consumption of salted-preserved fish, a traditional staple food in several NPC-endemic areas. Salted fish and other salted and preserved foods contain nitrosamines and nitrosamine precursors, knew animal carcinogens (Poirier et al., 1987; Fong and Chan, 1997). Many studied including the study in Northern Thailand reported that salted fish intake has been associated with the risk of NPC (Yu et al., 1986; Sriamporn et al., 1992; Armstrong et al., 1998; Yuan et al., 2000a; Zou et al., 2000). In contrast to most studies, we did not observed a positive association between NPC and consumption of salted fish. A case control study in Philippines also shows no association between NPC and salted fish consumption (West et al., 1993). Our dietary finding, however, should be interpreted with care, since it may cast doubt on the validity of the information obtained using food-frequency questionnaire.

The association between NPC and lower educational level was presented in this study. In previous studies, indicators of lower socioeconomic status and poor housing conditions were found to be positively associated with NPC in South-East Asia and Tunisia (Geser et al., 1978; Armstrong et al., 1978; Jeannel et al., 1990). This may indicate the existence of additional risk factor (e.g. early infections with EBV, diet or occupational factors) that are correlated with education. NPC case showed higher likelihood of having a history of chronic ear or nose conditions than control subjects. Our findings are in agreement with result of prior case control studies (Henderson et al., 1976; Yuan et al., 2000b; Friborg et al., 2007). The overall evidence thus suggests that the inflammatory and certain other benign conditions of the ear or nose predispose the nasopharyngeal mucosa to transformation on exposure to environmental carcinogens.

Several studies have associated wood dust with adenocarcinoma of the nasal cavities and paranasal sinuses (Yu and Henderson, 1996). Dust particles from wood occur frequently in Thai occupational environment, the number of wood processing industry is increasing over the past decade. Demers et al (1995) performed a pooled analysis of data from one UK and from US cohort studies on wood dust, and found excess NPC among furniture and plywood workers. But evidence relating NPC to wood dust has remained less clear. Our results confirm earlier observations in previous studies that NPC is associated with occupational exposures to wood dust (Sriamporn et al., 1992; Armstrong et al., 1998; Hildesheim et al., 2001). However, estimates of occupational exposure obtained from job title alone are prone to misclassification. Further studies on exposure assessment such as expert assessment or direct exposure measurement will be needed to investigate the possible role of wood dust in NPC development, the study is currently underway in our laboratory.

In summary, our study identified some risk factors for NPC in a Thai population, the results indicate that cigarette smoking, chronic ENT disease and exposure to wood dust might be associated with an increase risk of NPC. Lower education confirms a significant effect on increasing in risk of NPC. No associations were observed between salted fish intake or alcohol consumption and NPC risk.

Acknowledgements

We express our sincere thanks to all patients, recruited control subjects, doctors, nurses and paramedical personnel of National Cancer Institute and Regional Cancer Centers, Thailand. This work was supported by the Ministry of Public Health. The authors declare no conflicts of interest.

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