Tropical Gastroenterology 2010;31(1):34–36

Original Article

The assessment of probable relationship between lung cancer and Helicobacter pylori infection

Ramin Behroozian and Elvis Moradkhan

Department of Internal Medicine, Urmia University of Medical Sciences, Urmia, Iran

Correspondence:
Dr. Ramin Behroozian
Email: rbehroozian@gmail.com

ABSTRACT

Background: Many sero-epidemiological and case-control studies suggest that *H.pylori* infection may be associated with the development of lung cancer.
Aim: The objective of this study was to investigate the relation between lung cancer and *Helicobacter pylori* infection.
Methods: 66 consecutive patients with histologically confirmed, primary lung cancer and 66 controls were enrolled in this study. All enrolled subject underwent an enzyme-linked immunosorbent assay (ELISA) IgG serologic test for *H. pylori* diagnosis.
Results: The study included 66 histologically verified lung carcinoma (53 men and 13 women) with the median age of 59 years (range 30 to 87 years) and 66 controls (50 men and 16 women) with the median age of 58 years (range 27 to 88 years). The prevalence of *H.pylori* seropositivity was 73% (48/66) in lung cancer but only 51% (34/66) in controls. The odds ratio for the association of *H.pylori* and lung cancer was 2.51 (95% CI 1.14 – 5.54, P<0.05).
Conclusion: The results of our study show that the population of patients with lung cancer has a significantly higher rate of seropositivity for antibodies against *H.pylori* than the population of subjects without lung cancer.

KEYWORDS: *H.pylori* infection, Lung cancer

Introduction

Primary carcinoma of the lung is a major health problem with a generally grim prognosis. It is one of the most common causes of mortality in the world[1,2]. It is the most common cause of cancer death for both men and women and accounts for 28% of the overall cancer death rate[3]. The objective of this study was to investigate the relation between lung cancer and *H.pylori* infection.

Material and Method

This study was conducted at the Department of Pulmonary Medicine, of the Urmia University of Medical Sciences (U.M.S.U). Urmia is a city in North West of Iran in Middle East Asia.Between April 2006 and March 2007, 66 consecutive patients with histologically verified primary lung cancer were enrolled in the study. Lung carcinoma diagnosis was confirmed by fiber optic bronchoscopy and/or trans thoracic needle aspiration.

Exclusion criteria were: prior *Helicobacter* eradication therapy, consumption of acid suppressive drugs or antibiotics in the preceding 6 months, a history of vagotomy or operations on the upper gastrointestinal tract.

The control population included patients hospitalized for any other disease other than lung cancer. Exclusion criteria for control group were: prior Helicobacter eradication therapy, consumption of acid suppressive drugs or antibiotics in the preceding 6 months and history of vagotomy or operations on the upper gastrointestinal tract. We selected 66 controls and matched them with the patients for sex and age (within 2 years) and smoking habit.

All enrolled subjects (lung cancer patients and controls) underwent an enzyme-linked immunosorbent assay (ELISA) IgG serologic test for *H. pylori* diagnosis (I-Biological Laboratories Gmbh, Hamburg, Germany). This kit has a sensitivity of 100% and a specificity of 99.8%.

A positive, borderline or negative result was assigned when the concentration of IgG antibodies against *H. pylori* was greater than 12, between of 8-12 and less than 8, respectively. In the event of an equivocal result, a repeated test was performed on serum obtained 2 wks after the initial sampling.

Statistical analysis

The relation between lung cancer and *H.pylori* infection was assessed by Fisher's exact test. All results were compared among two groups by percentage and frequency tables and charts. In addition odds ratio (OR) and 95% confidence interval were estimated for percentage of lung cancer and H.pylori infection relationship. A p value of <0.05 was considered as significant. The statistical data analysis was performed with SPSS 10.

Results

This study was carried out on 66 histologically verified lung carcinoma patients (53 men and 13 women) with the median age of 59 years (range 30 to 87 years) and 66 controls (50 men and 16 women) with the median age of 58 years (range 27 to 88 years). The demographic data of both patients and controls are shown in **Table 1**.

Among the lung cancer patients, 25 (37.87%) had adenocarcinoma, 21 (31.82%) had squamous cell carcinoma, 16 (24.25%) had small cell cancer , 3 (4.54%) had large cell cancer and 1 (1.52%) had broncho alveolar carcinoma.

The majority of lung cancer patients were current cigarette smokers (more than 4 daily cigarettes during one last year) (55 patients, 83.3%) and 11 patients (16.7%) were ex-smokers or never smoked.

In the control group, 48 persons (72.72%) were current cigarette smoker and 18 (27.28%) persons were ex-smokers or never smoked.

There was no statistical difference in age, gender and smoking habit between the two groups (**Table1**).

The prevalence of *H.pylori* seropositivity was 3% (48/66) in patients with lung cancer but only 51% (34/66) in controls and this difference in *H.pylori* seropositivity between cancers and controls was statistically significant. The odds ratio for the association of *H.pylori* and lung cancer was 2.51 (95% CI = 1.14 – 5.54, P<0.05).

Table 1: Characteristics of patient group and control group

Parameter	Lung cancer (66)		Control (66)		P-value
	N	%	N	%	
Median age	59yrs		58yrs		0.7
Male gender	53	80.3	50	75.7	0.6
Current smoking	55	83.3	48	72.7	0.2
H.pylori seropositivity	48	72.7	34	51.5	0.01

Discussion

Lung cancer is one of the most common causes of mortality in the world. During the last 50 years, its incidence is dramatically increasing, not only in men but also in women[1]. It is the most common visceral malignancy accounting for about one third of all cancer deaths in men and more than 7% of all deaths in both sexes. Lung cancer has been strongly linked to cigarette smoking. It also occurs in association with occupational and environmental exposure to carcinogenic agents[1]. There are some other factors related to the development of lung cancer such as familial predisposition, genetic alteration, and more recently *H. pylori* infection[4-9]. *H. pylori* has co-existed with humans for thousands of years. However, because scientists believed the stomach was a sterile organ, this bacterium *was not* discovered until the 1980s[10].

Some previous studies investigated the association between *H. pylori* seropositivity and lung cancer. Ece et al, found a 93% seroprevalence of antibodies against *H. pylori* in 40 consecutive *patients* with lung cancer and a 42% seroprevalence in 12 control subjects[2]. In a case-control study, Roussos et al, found a significant association between chronic bronchitis and *H. pylori*[11]. Philippou et al[6] failed to establish an association between *H. pylori* infection and lung cancer. They reported that seropositivity for *H. pylori* did not differ significantly between patients with lung cancer and controls (61.1% vs. 55.9% P> 0.05).

The results of our study showed that the population of patients with lung cancer has a significantly higher rate of seropositivity for antibodies against *H.pylori* (48 of 66) than the population of subjects without lung cancer (34 of 66). (OR=2.51, 95%CI= 1.14 – 5.54 P<0.05). However, such association was not confirmed in Najafizadeh et al study in Iran performed of 40 patients with lung cancer, which may be due to small sample size[12].

H. pylori infection in the stomach is known to be accompanied by a markedly enhanced and prolonged release of gastrin that has been suggested to account for the development of gastric cancer and has been shown to express with COX-2[8]. Furthermore, an over expression of cyclooxygenase-2 was reported in lung cancer by numerous investigators suggesting that this enzyme could be responsible for abundant release of eicosanoids, cell proliferation, angiogenesis and reduction in apoptosis, similarly as in gastric cancer[8].

H. pylori infection is accompanied by an increased plasma level of gastrin, suggesting that this hormone could contribute to the lung carcinogenesis by inducing higher mucosal cell proliferation of bronchial epithelium leading to atrophy and induction of COX-2[13,14]. Th finding that lung cancers exhibit higher expression and content of gastrin and its receptors is akin to up regulation of gastrin biosynthesis already described for gastric cancers and colorectal cancers[15]. As gastrin is known to be the most potent mucosal growth promoting factor in gastrointestinal tract (and possibly also in the bronchial mucosa), it is tempting to assume that this hormone could play a key role in the initiation and the progression of cancer disease both in the gastrointestinal tract and the lungs that embryologically originating from the same endoderm tube[8].

The reason for the higher prevalence of *H.pylori* infection in the lung cancer patients is not apparent but the fact that the majority of cancer patients were smokers, who are known to have higher *H.pylori* infection rate.Although smoking is thought to be related to *H.pylori* infection, some studies supporting our findings, showed no significant relation between *H.pylori* seroconversion and smoking[16].

In our study, 72.7% of control subjects were smokers (more than 4 daily cigarettes during last year); however, *H. pylori* seropositivity was significantly lower in control group than case one. So, *H. pylori* infection by itself may be a risk factor for lung cancer. Increased plasma level of gastrin which is accompanied by *H.pylori* infection may contribute to the lung cancerogenesis by inducing mucosal cell proliferation of

bronchial epithelium[12].

The main limitation of this study was selection of control group. The control group population consisted of patients admitted for other diseases and were not healthy adults.

Our results suggest that *H.pylori* infection may have an association with lung cancer. However, further studies with larger sample size are needed to further elucidate the potential pathogenetic relationship between *H.pylori* infection and lung cancer.

Acknowledgements

The authors would like to thank Farzan Institute for Research and Technology for technical assistance.

References

1. Minna JD. Neoplasms of the lung. In: Kasper DL, eds. Harrison's Principles of Internal Medicine 16th Ed. *New York: Mc Graw-Hill;* 2005. p. 506–15.
2. Ece F, F Hatabay N, Erdal N, Gedik C, Guney G, Aksoy F. Does Helicobacter pylori infection play a role in lung cancer? *Respir Med*. 2005;**99**:1258–62.
3. Slavis BS, Brigham KL. Neoplastic diseases of the lung. In: Andreoli TE, Carpenter CCJ, Griggs RC, Loscalzo J, eds. Cecil Essential of Medicine. 6th Ed. *Philadelphia, Pa: Saunders*; 2004. p. 213–16.
4. Roussos A, Philippou N, Gourgoulianis KI. Helicobacter pylori infection and Respiratory disease: a review. *World J Gastroenterol*. 2003;**9**:5–8.
5. Kanbay M, Gur G, Akcay S, Yilmaz U. Helicobacter pylori seroprevalence in patients with chronic bronchitis. *Respir Med*. 2005;**99**:1213–6.
6. Philippou N, Koursarakos P, Anastasakou E, Krietsepi V, Mavrea S, Roussos A et al. Helicobacter pylori seroprevalence in patients with lung cancer. *World J Gastroenterol*. 2004;**10**:3342–4.
7. Tsang KW, Lam SK. Helicobacter pylori and extra-digestive diseases. *J Gastroenterol Hepatol*. 1999;**14**:844–50.
8. Gocyk W, Niklinski T, Olechnowicz H, Duda A, Bielanski W, Konturek PC, et al. Helicobacter pylori, gastrin and cyclooxygenase-2 in lung cancer. *Med Sci Monit*. 2000;**6**:1085–92.
9. Tsang KW, Lam SK, Lam WK, Kalberg J, Wong BC, Hu WH, et al. High seroprevalence of Helicobacter pylori in active bronchiectasis. *Am J Respir Crit Care Med*. 1998;**158**:1047–51.
10. Vakil N, Fennerty B. The economics of eradicating Helicobacter pylori infection in duodenal ulcer disease. *Am J Med*. 1996;**100**:60S–63S.
11. Roussos A, Tsimpoukas F, Anastasakou E, Alepopoulou D, Paizis I, Philippou N. Helicobacter pylori seroprevalence in patients with chronic bronchitis. *J Gastroentrol*. 2002;**37**:332–5.
12. Najafizadeh K, Falah Tafti S, Shiehmorteza M, Saloor M, Jamali M. H pylori seroprevalence in patients with lung cancer. *World J Gastroenterol*. 2007;**13**:2349–51.
13. Wolff H, Saukkonen K, Antiila S, Karjalainen A, Vainio H, Ristimaki A. Expression of cyclooxygenase-2 in human lung carcinoma. *Cancer Res*. 1998;**58**:4997–5001.
14. Hida T, Yatabe Y, Achiwa H, Muramatsu H, Kozaki K, Nakamura S, et al. Increased expression of cyclooxygenase-2 occurs frequently in human lung cancers, specifically in adenocarcinomas. *Cancer Res*. 1998;**58**:3761–4.
15. Konturek PC, Konturek SJ, BielaÄski W, Karczewska E, Pierzchalski P, Duda A. Role of gastrin in gastric cancerogenesis in Helicobacter pylori infected humans. *J Physiol Pharmacol*. 1999;**50**:857–73.
16. Gikas A, Triantafillidis JK, Apostolidis N, Mallas E, Peros G, Androulakis G. Relationship of smoking and coffee and alcohol consumption with seroconvertion to Hhelicobacter pylori, a longitudinal study in hospital workers. *J Gastroentrol Hepatol*. 2004;**19**:927–33.