

RESEARCH ARTICLE

Serum Zinc Status and *Helicobacter Pylori* Infection in Gastric Disease Patients

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Abstract

The role of *Helicobacter pylori* status and serum zinc value in gastric disease patients and healthy controls were investigated. Cases used in this work were 45 gastric cancer patients, 44 with peptic ulcers, 52 suffering gastritis and 64 healthy controls, all diagnosed histologically with the controls undergoing medical checkups. *Helicobacter pylori* status and serum levels of Zn were determined by ¹³C-urea breath test and flame atomic absorption spectrophotometer, respectively. Our study showed that *Helicobacter pylori* infection has no change in gastritis, peptic ulcer and gastric cancer group, on the contrast, serum levels of Zn were significantly reduced in gastritis, peptic ulcer and gastric cancer group, compared with healthy controls, and the higher the Zn levels are, the more increased risk of gastric cancer. *Helicobacter pylori* infection is a cause of gastritis, peptic ulcers and even gastric cancer, while serum zinc level is an indicator of protection of gastric membranes against damage.

Keywords: *Helicobacter pylori* - serum zinc - gastric cancer - peptic ulcers - gastritis

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Introduction

Gastric cancer is one of the most frequent cancers in the worldwide. It is often asymptomatic or causes only nonspecific symptoms in its early stages. By the time symptoms occur, the cancer has often reached an advanced stage. This is one of the main reasons for its poor prognosis. Gastric cancer is the second leading cause of death from cancer. It can develop in any part of the stomach and spread to other organs. A significant increase in its incidence has been reported for both men and women over the last 2 decades (Amedei et al., 2011; Jang et al., 2011; Meyer and Wilke, 2011).

Helicobacter pylori (*H. pylori*) infection is the most common bacterial infection in humans. It is regarded as a major etiologic factor in the development of chronic gastritis, peptic ulcer and gastric cancer (Lopez-Saez et al., 2010). In more detail, *H. pylori* are the main risk factor in 65–80% of gastric cancers, but in only 2% of such infections (You et al., 2000; Testerman et al., 2006; Vilchis et al., 2009; Janjetic et al., 2010; Zamani et al., 2011). That is to say, despite the worldwide distribution of *H. pylori* infection in patients with gastric disease, only a few number of infected individuals develop gastric cancer. It is important to clarify other factors that may determine risk among those infected with *H. pylori* (Hisaki et al., 1988; Lin et al., 2002).

It is reported that gastric cancer may be caused by reactive oxygen species (ROS), and dietary antioxidants,

such as zinc, may protect against this disease (Wu et al., 2004; Mazdak et al., 2010). Superoxide dismutase (SOD) plays a key role in the detoxification of superoxide radicals. There are at least two forms SOD, cytoplasmic copper/zinc SOD (Cu/Zinc SOD) and mitochondrial manganese (Mn SOD), Cu/Zinc SOD forms a crucial part of the cellular antioxidant defense mechanism, who catalyzes the dismutation reaction of the toxic superoxide radical to molecular oxygen and hydrogen peroxide (Milde et al., 2005; Prasad, 2009). As a trace element exist in all body tissues and fluids, Zinc is essential for the survival and function of cells. The gastritis may be impaired in conditions of zinc deficiency, depending on the severity of the deficiency. Zinc deficiency may cause the severity of infectious diseases and zinc supplementation can reduce the incidence of infections, and the severity of the symptoms (Matsukura and Tanaka, 2000). Low serum zinc concentrations may be associated with inflammatory bowel disease (IBD) 5 and gastric mucosa inflammation induced by *H. pylori* (Akcem, 2010).

The aim of our study was to examine the association of serum levels of Zinc, *H. pylori* infection and gastric cancer risk.

Materials and Methods

Patients

This study was carried out in 45 patients of gastric cancer and 44 matched (age and sex) patients of peptic

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Table 1. Demographic Characteristics, H. Pylori Status and Serum Zinc Value in Patients and Control Group

Groups	Serum Zinc ($\mu\text{mol/L}$)*		P	Sex		χ^2	P	Age*	P
	H. pylori (+)	H. pylori (-)		Male	Female				
Control	18.9 \pm 3.9	18.3 \pm 4.0	0.63	32	18	0.40	0.94	49.7 \pm 6.3	0.98
Gastritis	16.7 \pm 3.8	16.8 \pm 4.1	0.93	34	15			49.1 \pm 6.0	
Peptic ulcer	13.9 \pm 2.8	14.0 \pm 2.7	0.95	30	15			49.4 \pm 6.4	
Gastric cancer	13.7 \pm 2.9	13.8 \pm 2.1	0.87	31	14			49.4 \pm 5.7	

*X \pm SD**Table 2. Serum Zinc Value in Patients and Control Group**

Groups	Serum Zinc ($\mu\text{mol/L}$)*	ANOVA		t-Test P-value			
		F	P-value	Gastric cancer	Peptic ulcer	Gastritis	Control
Control	18.7 \pm 3.9	24.5	0.00	0.00	0.00	0.01	-
Gastritis	16.8 \pm 3.8			0.00	0.00	-	-
Peptic ulcer	14.0 \pm 2.8			0.68	-	-	-
Gastric cancer	13.7 \pm 2.7			-	-	-	-

*X \pm SD

ulcer, 52 matched patients of gastritis, 64 matched healthy control. All cases were the patients with gastric disease who were referred to the Department of Gastroenterology, Tianjin Union Medicine Center, Tianjin, China, between 2010 and 2012. For evaluation of upper gastrointestinal symptoms, an endoscopy was performed on all cases and the diagnosis was confirmed by an examination of the resection or biopsy specimen. Control subjects were recruited from a group of routine health examination people who underwent medical checkups at a health promotion center in the same area and same time.

13C-urea Breath Test

Patients were instructed to fast for at least 6 hours before the diagnostic test was performed. By the method of ¹³C-urea breath test, A change of >3.5% in the delta over baseline values was considered positive. The ¹³C-UBT is a highly accurate diagnostic test, with values of sensitivity and specificity >95%.

Serum Zinc Test

Venous blood samples were obtained in the morning before performance of the ¹³C-UBT. Serum samples of cases and controls were collected in the same method and stored -80 °C until analysis. The serum concentration of Zinc was measured with flame atomic absorption spectrophotometer. Extensive precautions were taken for both collection and subsequent handling of serum in order to avoid or minimize trace elements contamination. All assays were performed by laboratory personnel who were blinded to the case/control status.

Statistic

SPSS software program (version 8.0) has been used for data analysis. To compare the serum zinc value of patients groups and control group, 1-way ANOVA followed by student's t-test has been done. P-value<0.05 is considered as significant difference.

Results

The Demographic characteristics, H. pylori status

and serum zinc value in patients and control group are presented in Table 1. 45 patients of gastric cancer, 45 matched (age and sex) patients of peptic ulcer, 49 matched patients of gastritis, were screened for the study and 50 matched healthy people were randomized to control group. The average age of patients was 49.4 \pm 5.7, 49.4 \pm 6.4, 49.1 \pm 6.0 years, respectively compared with 49.7 \pm 6.3 years of control group. The age interval of all patients and controls is from 40 to 60 years old. 68.9%, 66.7%, 69.4% of patients and 64.0% of control groups were male. The differences between 4 groups are not significant.

When considered H. pylori status, Table 1 also shows mean values of the zinc status according to H. pylori infection. No significant differences were found for H. pylori positive and negative patients in any diseases and control group. Table 2 shows the selected characteristics of case and control subjects. When compared to the results of serum zinc levels in patients and control group, the serum zinc levels in patients were found to be 16.8 \pm 3.8 mg/L, 14.0 \pm 2.8 mg/L, and 13.7 \pm 2.67 mg/L respectively. P-value (0.05) was considered significantly different compare with 18.7 \pm 3.9 mg/L in control group. That Zinc serum level in gastritis patients is lower than those in control group, more lower in peptic ulcer patients and gastric cancer patients. The same serum zinc levels tendency happened in peptic ulcer patients and gastric cancer patients. The median level of serum Zinc was significantly higher in cases than in controls. The risk of gastric cancer is positively associated with serum levels of Zinc, and the trend is statistically significant (trend P 0.05) (Table 2). That is to say the higher the serum levels of Zinc, the higher the risk (trend P 0.05) (Table 2). There was a significant association between serum levels of Zinc and an increased risk of gastric cancers.

Discussion

Our data indicates that serum levels of Zinc were significantly lower in gastric cancer patients than in health controls. The risk of gastric cancer increased substantially as serum Zinc levels decreased. Zinc might involve in gastritis and peptic ulcer progression, could be involved

in the genesis of gastric cancer.

The mechanism by which Zinc interferes with gastric carcinogenesis has not been clarified (Martin-Lagos et al., 1997; Lamson and Brignall, 2001; Abnet et al., 2005; Zarghami et al., 2005; Khorasani et al., 2008; Sadat et al., 2008). Zinc may bring contribute to some cause to the host defense mechanism by maintaining the structure and function of the membrane barrier (Newberne, 1987; Finamore et al., 2008), that is especially important in the gastro-intestine tract, which is continuously exposed to plenty of pathogens and noxious agents. The manner in which the gastro-intestinal epithelium constitutes a barrier involves intercellular junctional complexes between neighboring cells that provide a continuous seal around the apical region of the cells. It has been reported that there is a neutrophil accumulation within epithelial crypts and in the gastro-intestinal lumen associated with gastro-intestinal disease and epithelial injury. Gut membrane injury resulted from zinc deficiency is associated with inflammatory cell infiltration. It is reasonable to find that patients with chronic intestinal permeability disorders may combine with a reduced level of mucosal zinc. Zinc deficiency may affect the intercellular junctional complexes structure of gastro-intestinal epithelial cells and result in consequently allow a more extensive migration of neutrophils. Depletion of zinc strongly destroys membrane barrier function and integrity, induces an increase in neutrophil accumulation, and starts a positive regulation of chemokines that plays an important role in neutrophil migration and inflammatory development (Dovhanj et al., 2009; Christudoss et al., 2010).

In this study, we found that, in the point of view of gastric membrane, healthy Control, gastritis patients, peptic ulcer patients and gastric cancer patients is a set of process indicating the severity of the destroy of gastric membrane. Our data indicates the more sever of the damage of gastric membrane, the lower the serum Zinc level. The same serum zinc levels tendency happened in peptic ulcer patients and gastric cancer patients. It might be the severity of gastric membrane in both groups was similar. On the other hand, we do not find a statistically significant difference in serum levels of Zinc between control subjects infected with *H. pylori* and those not infected with *H. pylori*. Same findings happened in gastritis patients, peptic ulcer patients and gastric cancer patients. *H. pylori* infection seemed to have nothing to do with gastritis, peptic ulcer and gastric cancer. Actually *H. pylori* infection is a cause of gastritis, peptic ulcer and even gastric cancer, serum Zinc level is an indicator of the damage of gastric membrane, or a protector of gastric membrane.

So it is very important for those healthy people who have been infected with *H. pylori*, to have enough Zinc intake to protect the destruction of *H. pylori* to the gastric membrane (Andrew, 1979; Memon et al., 2007; Dovhanj et al., 2010; Janjetic et al., 2010; Alipour et al., 2011).

In conclusion, our results indicates the important role played by zinc intake in the maintenance of membrane barrier function and in controlling inflammatory reactions since the depletion of zinc causes disruption of gastric membrane Our study showed that, serum levels of

Zinc were significantly lower in gastric cancer patients, compared with healthy controls, and decreased serum levels of Zinc may be associated with an increased risk of gastric cancer in people infected with *H. pylori*. Actually *H. pylori* infection is a cause of gastritis, peptic ulcer and even gastric cancer, serum Zinc level is an indicator of the damage of gastric membrane, or a protector of gastric membrane. The clinical implication of our finding is that in the early diagnosis of gastric cancer we should pay more attention to those who have both *H. pylori* infection and decreased serum Zinc.

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