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Nutrition and *Helicobacter pylori* infection in gastric disease

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Abstract

H. pylori is a highly prevalent bacterial infection among humans. It is considered the major etiological factor in the development of chronic gastritis, peptic ulcers, and stomach cancer. Nutritional therapy is important for the prevention of gastritis, as well as for reducing stomach irritation (irritation) in the treatment of gastritis, *and it* plays an important role by helping to eradicate or strengthen the stomach wall. Chronic gastritis should be diagnosed before it progresses and causes fatal diseases such as peptic ulcer or cancer, and it should be treated with both a healthy diet and appropriate medications.

Keywords: Chronic Gastritis; Micronutrients; Atrophic Gastritis; Probiotics; Vitamins

1. Introduction

H. pylori is a highly prevalent bacterial infection among humans. It is considered the major etiological factor in the development of chronic gastritis, peptic ulcers, and stomach cancer (1). A minority of these patients develop more significant complications, such as peptic or duodenal ulcer, MALT lymphoma, or stomach cancer, although nearly all *H. pylori*-infected hosts develop gastritis. *H. pylori* is associated with approximately 75% of all stomach cancers and 5.5% of all cancers worldwide (2). The development of atrophic gastritis, intestinal metaplasia, dysplasia, and ultimately stomach cancer is referred to as the "Correa pathway", which is based on chronic inflammation of the gastric mucosa that triggers a series of genotypic disorders ultimately leading to carcinogenesis (3-6). In addition, recent research has linked HP infection to non-gastrointestinal diseases, including hematological (persistent iron deficiency anemia, idiopathic thrombocytopenic purpura), neurological (stroke, Parkinson's disease, Alzheimer's disease), and cardiovascular (ischemic heart disease) conditions (7).

2. Micronutrients and *H. pylori*

2.1. Iron and *H. pylori*

Iron is an essential growth factor for *H. pylori*. *H. pylori* possesses intracellular storage proteins with properties similar to ferritin, as well as outer membrane proteins that are involved in the bacterial uptake of iron (8). The association between *H. pylori* infection and iron deficiency anemia is well established. The Maastricht Dec III European guidelines strongly recommend a test and treatment approach for *H. pylori* infection in patients with unexplained sideropenic anemia (9).

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H. pylori infection can contribute to iron deficiency anemia through various mechanisms. First, it can cause hypochlorhydria, leading to the conversion of ascorbic acid to dehydroascorbic acid. Additionally, it can cause the ferric form of iron to be reduced to the ferrous form, which makes it less available for absorption. These processes ultimately lead to decreased iron absorption, which can lead to anemia (10,11).

2.2. Vitamin B12

Vitamin B12, also known as cobalamin, is an essential nutrient that cannot be synthesized by humans and must be obtained through dietary sources. This vitamin is primarily found in animal-derived foods such as meat, poultry, fish, shellfish, eggs, and dairy products. Vegetarians and vegans are at a higher risk of developing vitamin B12 deficiency due to limited dietary intake. Many studies have examined the molecular biology of vitamin B12 deficiency (12,13). In vitamin B12 deficiency, purine and pyrimidine cannot be synthesized and megaloblastic anemia develops as a result. The accumulation of methylmalonyl-CoA in the body is also associated with neurological findings(14). Vitamin B12 taken with a diet binds to proteins. Vitamin B12, which is separated from protein in the acidic environment of the stomach, is bound by the transporter haptocorin (Protein-R), also called as transcobalamin I, found in salivary secretion. Approximately 80% of vitamin B12 in the circulation is also found to be due to haptocorin. In the acidic environment of the stomach, the affinity of haptocorin for vitamin B12 is greater than intrinsic factor (IF). After the haptocorin-vitamin B12 complex passes into the small intestine, it is partially digested by pancreatic enzymes here and combines with IF, whose affinity for vitamin B12 increases in the alkaline environment of the intestine. Additionally, IF is resistant to digestion by pancreatic enzymes. The vitamin B12-IF complex, which reaches the terminal ileum, is taken into the cell by phagocytosis and binds to its specific receptors (12,13). Because of these pathogenic mechanisms, the stomach plays an important role in vitamin B12 metabolism, and B12 metabolism is also affected in gastric diseases.

H. pylori infection can lead to pernicious anemia by disrupting the absorption of vitamin B12 (15,16). In an adult study conducted by Kaptan et al. (16), the HP positivity rate was 56% in patients undergoing endoscopy due to B12 deficiency. In this study, HP eradication led to an increase in B12 levels in 40% of the patients, and the researchers noted that endoscopy was performed in patients with B12 deficiency, and HP treatment alone was sufficient in many cases to increase B12 levels. Tamura et al. (17) demonstrated that the atrophic gastritis score was higher and vitamin B12 levels were lower in the HP-positive group than in the HP-negative group. In this study, low vitamin B12 levels were thought to be due to decreased gastric acid secretion secondary to atrophic gastritis(17). However, in a study conducted by Akçam et al.(18), HP infection can cause vitamin B12 deficiency even without causing atrophic gastritis. Although studies have demonstrated a substantial correlation between HP infection and vitamin B12 deficiency, the presence of atrophic gastritis does not influence this relationship. Similarly, HP-positive gastritis may be the only endoscopic finding in patients with vitamin B12 deficiency (19). However, in a study conducted by Kalkan et al. in elderly people with non-atrophic gastritis, the factors affecting vitamin B12 deficiency were examined. 1256 patients over the age of 60 who were diagnosed with non-atrophic gastritis were divided into two groups as 759 people with an average serum B12 level of 339 pg/ml and 497 people with an average serum B12 level of 180 pg/ml (normal blood value of B12: 220 - 940 pg/ml). As a result of the study; *H. pylori*, neutrophil activity, intestinal metaplasia and inflammation frequency were found to be significantly higher in the second group with low B12 level than in the first group (20).

2.3. Folate

In adults, there is a negative association between *H. pylori* infection and folate metabolism. This may be attributed to a reduction in folate absorption resulting from decreased vitamin C concentration in the gastric fluid or an increase in intragastric pH secondary to *H. pylori* infection (21).

2.4. Selenium

Selenium is a cofactor of glutathione peroxidase, which prevents oxidative damage to membranes. The concentration of selenium in the antral mucosa of patients with atrophic gastritis is considerably reduced. Selenium deficiency can cause various complications such as immune response disorders, susceptibility to infection, and malignancies. (22,23). Wu et al. have proposed that the reduction in the level of selenium can be considered as evidence of its protective effect against *H. pylori* infection following eradication of the bacterium (24).

2.5. Zinc

Zinc is a crucial micronutrient for cellular survival and function. Zinc deficiency has been linked to increased severity of infectious diseases, while zinc supplementation has been shown to reduce the incidence of infections and the severity of associated symptoms (25). It may be associated with the low serum zinc concentrations, inflammatory bowel disease (IBD) and the inflammation of the gastric mucosa caused by *H. pylori* (26). In addition to its role in regulating the secretion of endotoxins and cytotoxins, zinc has been shown to be an important cofactor for *H. pylori* urease and nickel-

iron hydrogenase (Ni, Fe-hydrogenase) enzymes, which are critical for the bacteria's survival in the low pH environment of the stomach (27-29). Zinc deficiency can affect the structure of the intercellular junction complexes of gastrointestinal epithelial cells and, as a result, allows neutrophils to migrate more extensively. Zinc insufficiency has been shown to severely compromise the integrity and function of cell membranes. This can lead to increased accumulation of neutrophils and upregulation of chemokines, which play a crucial role in the migration of neutrophils and the development of inflammation (30,31). Therefore, it is very important that healthy people infected with *H. pylori* have sufficient Zinc intake to prevent the destruction of H.pylori to the gastric membrane(32-36).

2.6. Cu

In the literature, no significant differences in serum Cu levels have been reported in most studies (37,38). Ozturk et al. Children with H.pylori infection reported a decrease in serum Cu (but not at significant levels).(39). In their studies, no difference was observed in serum Se levels as well as an increase in serum Zn levels (39). Hacibekiroğlu et al. reported no significant relationship between H. pylori antibodies and serum Fr, Cu, or Zn levels (37). Wu et al. reported that there is no significant difference between serum Zn, Se, and Cu levels compared with control subjects in people infected with H. pylori (40).

3. Vitamins

3.1. β-carotene

B-carotene is the most abundant form of pro-vitamin A and is commonly found in fruits and vegetables. It can neutralize reactive oxygen compounds produced by oxidative stress together with its metabolites. The gastric mucosal β-carotene concentration was found to be significantly reduced in patients with gastric atrophy and intestinal metaplasia. (41).

3.2. Vitamin C

Ascorbic acid, a water-soluble antioxidant, can neutralize mutagens generated by nitrite and protect against carcinogenesis (42). A study with more than 1100 participants revealed that *H. pylori*-infected patients had a 20% lower plasma concentration of vitamin C than negative controls (43). Hypochlorhydria can convert ascorbic acid to dehydroascorbic acid (less active form) (44).

3.3. Vitamin E

Vitamin E contains two classes of compounds, tocopherols and tocotrienols. α-tocopherol is the most common form, representing the most important fat-soluble antioxidant of biological membranes. In patients with H.pylori infection, the mucosal concentration of α-tocopherol of the corpus is lower than in the antrum or duodenum (45); probably this phenomenon reflects the mobilization of antioxidant defenses to large areas of the stomach(46).

Vitamin C is also involved in the conversion of folate to tetrahydrofolic acid (47). Vitamin C deficiency can worsen folate deficiency. As a result, the effects of *H. pylori* infection on human vitamin levels are not isolated, and there may be interactions between different vitamins (48-51). Vitamin D and the vitamin D receptor may trigger immune responses and contribute to the anti-*H. pylori* activity when combined (52, 53). In a meta–analysis study in which 10 studies investigating the effectiveness of vitamin C and / or E supplements in the treatment of H.pylori infection of Ochoa et al. were evaluated, it was found that these vitamin supplements did not have a significant effect on bacterial eradication(54).

4. *H. pylori* and Nutrition

One of the risk factors for stomach cancer is *H. pylori* the relationship between nutrition and is being intensively researched. While some nutrients are a risk factor for this bacterium, others are thought to be protective against bacteria or help in the eradication of bacteria (55).

4.1. Vegetable Consumption

Consumption of vegetables, especially non-starchy vegetables, is protective against stomach cancer. In vitro studies have shown the direct bactericidal effect of sulfarone found in broccoli *H. pylori* and that it inactivates urease (56,57). Yanaka et al.in the work of (57) they have done, *H. pylori* 48 individuals with the infection consumed 70 g (about 1 cup) of sulforaphane-rich broccoli sprouts per day for eight weeks, and it was found that inflammation decreased in these individuals. Research has shown that broccoli sprout, known as sulforaphane, has a chemical and *H. pylori* it has shown

that it has an anti-bacterial effect related to. Epidemiological studies have also reported a negative correlation between gastric cancer and radish consumption. The anti-H. pylori effects of radish, cabbage, and okra have been found in some studies. Garlic is also anti-oxidant and antimicrobial due to its antimicrobial - *H. pylori* it shows the effect (56).

4.2. Fruit Consumption

Fruits have protective properties against H.Pylori with antioxidants they contained, especially vitamin C, which is a powerful antioxidant. Vitamin C (ascorbic acid) is not synthesized in humans; it is taken up with nutrients and increases stomach acidity. Thus, both the activation of *H. pylori* and the formation of nitrosamines from nitrates and nitrites in the stomach are suppressed, and the development of stomach cancer is prevented. However, it was not proven that vitamin C has a significant effect on H. pylori treatment in these studies. Ochoa et al.of *H. pylori* in a meta–analysis study in which 10 studies investigating the effectiveness of vitamin C and/or E supplements in the H.pylori infection treatment of Ochoa et al. were evaluated, it was found that these vitamin supplements did not have a significant effect on bacterial eradication(54). In contrast, it has been found that ascorbic acid levels are low in gastric fluids of gastritis patients (58). It is stated that dysplasia occurs as a result of oxidation of cells in the mucosa in ascorbic acid deficiency and gradually causes stomach cancer. For this reason, it is recommended to eat fresh vegetables and fruits containing vitamin C at every meal or take 100-200 mg of vitamin C every day. However, in a community-based double-blind randomized controlled trial in the Japanese population, vitamin C supplementation did not have a strong effect on the reduction of infections in patients with chronic gastritis in an area with a high incidence of stomach cancer (59).

Capsaicin is an effective antioxidant against H.pylori. It is found in cayenne pepper and paprika. Animal studies have shown that capsaicin is effective in healing gastrointestinal lesions. Capsaicin is an effective antioxidant against H.pylori. It is found in cayenne pepper and paprika. Animal studies have shown that capsaicin is effective in healing gastrointestinal lesions. In human studies, these substances have been shown to be gastroprotective only in people with aspirin-induced lesions (60).

4.3. Cholesterol Intake

In a study by Ikezaki et al. (61), to investigate the effect of *H. pylori* eradication treatment on nutritional intake, serum *H. pylori* antibodies were measured and a nutrient frequency questionnaire was administered. Of the 389 patients who underwent one week of *H. pylori* eradication treatment, 60.4% were found to have eradicated the bacterium at the eight-week follow-up measurements (235/389). Factors associated with treatment failure include an increase in age, higher concentrations of CRP, and higher dietary cholesterol or egg intake. The results of this study, gastritis or duodenal ulcer *H. pylori* - successful use of high egg and fish intake in positive cases *H. pylori* it has shown that it may be negatively associated with eradication therapy.

4.4. Salty Nutrition

A study utilizing a Mongolian gerbil model found that animals infected with H.pylori and fed a high-salt diet exhibited increased inflammation compared to infected animals fed a normal diet (62). This deterioration in tissue structure and inflammation is caused by H.pylori is accompanied by an increase in hypochlorydia in animals fed with excessive salt (62). Studies have shown that alterations in salt concentration affect various components of H.pylori. For instance, HopQ, which is associated with H.pylori virulence, is upregulated when the bacterium is exposed to high salt stress. On the other hand, VacA, which is a cytotoxin produced by H.pylori, is upregulated when exposed to low salt conditions. In addition, changes in salt concentration have been found to impact the production of the outer membrane protein. These studies suggest that changes in salt consumption can affect both the host and H. pylori, and the convergence of these changes may contribute to the development of carcinogenesis.

4.5. Probiotics

Probiotics are defined by the Food and Agriculture Organization (FAO) and the World Health Organization (WHO) as "living microorganisms that provide a health benefit to the host when administered in sufficient quantities". They are necessary for an optimal digestive system and are protective against many diseases. There are also bactericidal effects. in a meta-analysis in which 33 clinical studies were evaluated, in groups taking probiotic supplements *H. pylori* a significant increase in eradication has been observed (56). At the same time, yoghurts containing Lactobacillus and Bifidobacterium cultures have been shown to reduce infection levels and increase the effectiveness of traditional antibiotic and acid inhibitor treatments for gastritis and ulcers (64).

The most commonly used probiotic strains for H.pylori infection are Lactobacillus johnsonii La1 (65-67). Lactobacilli, which are the dominant intestinal bacteria, prevents H.pylori from adhering to gastric epithelial cells in vitro. The administration of exogenous lactobacilli may aid in the eradication of *H. pylori* by regulating the secretion of endotoxins

and cytotoxins. Other probiotic strains, such as Lactobacillus acidophilus, Bifidobacterium lactis, and Saccharomyces boulardii, have also been used alone or in conjunction with antibiotics specific to *H. pylori*. Meta-analytic studies have recommended the use of Saccharomyces boulardii or Lactobacillus species supplementation in combination with standard triple treatment to enhance the efficacy of *H. pylori* eradication (68,69). Cats et al. (70) conducted a study on 14 patients infected with *H. pylori* and administered L. acidophilus (108 CFU) for three weeks. The results showed that the growth of *H. pylori* was inhibited in 64% of the participants. Similarly, Wang et al. (81) administered Bifidobacterium animalis and L. acidophilus (1010 CFU) twice daily to 59 volunteers for six weeks (71). The researchers observed that regular consumption of yogurt containing Bifidobacterium animalis and L. acidophilus had a suppressive effect on *H. pylori* infection.

Although there are studies showing that eradication success increases with the addition of probiotic-containing yogurts to treatment (72,73) studies have also been conducted that say the opposite (74-76).

5. Alternative treatments for peptic ulcer with no proven effectiveness

Research has shown that certain chemical compounds, such as flavonoids and antioxidants, found in boldo and carqueja leaves are associated with the various activities attributed to these plants. However, the efficacy of these teas in treating peptic ulcers has not been scientifically established (77).

In a study by Mentz and Schenkel (78), in which they evaluated plants whose effects were widely known to prove scientifically, Symphytum Officinale L. Although plants such as (comfrey) have no proven effectiveness, they have observed that they can be harmful due to pyrrolizidine alkaloids.

Flavonoids increase blood flow in the mucosa. It also stimulates the production of glycoprotein, glycolipid and mucin in the gastric mucosa (79). A case-control study conducted in China with 299 cases and 433 healthy controls demonstrated that consumption of green tea was associated with a protective effect against chronic gastric disease and a reduced risk of progression to gastric cancer (80). Similarly, a Japanese research reveals that green tea consumption protected against chronic atrophic gastritis and that the polyphenols in green tea prevented the release of proinflammatory cytokines (81).

A high-fiber diet acts as an intermediate, reducing the concentration of gastric juices in the stomach, preventing irritation of the mucous membranes (82).

6. Recommendations for Nutritional Therapy in Gastritis

Nutritional therapy is important for the prevention of gastritis, as well as reducing stomach irritation (irritation) in the treatment of gastritis, *H. pylori* it plays an important role by helping its eradication or strengthening the stomach wall. In general, nutritional recommendations for patients with gastritis can be summarized as follows:

- The food should be consumed slowly.
- Foods causing indigestion should not be consumed.
- Fresh vegetables and fruits should be consumed every day to support vitamin C intake
- Meals should be eaten little, often and regularly.
- The consumption of dark tea, alcohol, coffee, roasts, spices, ketchup, and mustard should be restricted.
- Smoking and alcohol consumption should be prohibited.
- Sweet, pastries and carbonated drinks should not be consumed.
- It is necessary that food is not too hot or cold.
- Curd and other cheeses can be eaten freely.
- Meals should be eaten at least two hours before going to bed at night.

• 8-10 cups of water should be consumed daily, but should not be taken with meals (83). Carrot juice combined with spinach juice is considered extremely useful in the treatment of gastritis (84). In this combination, 200 mL spinach juice and 300 mL carrot juice are mixed. Many different foods should not be mixed in the same meal. Meals should be eaten at least two hours before going to bed at night. In chronic gastritis, the gastric juice flow is insufficient, and foods that require chewing for a long time create a larger flow in the gastric juice. As a nutritional treatment, a diet with little pulp, non-stimulant, energy, and other nutrients (especially protein, vitamins A, C, E, and iron) is sufficient, the number of meals is high, and the proportion of nutrients is low (85). Ferri-De-Barros et al. (86) reported that chronic alcohol consumption can lead to various gastrointestinal problems, including esophagitis, chronic pancreatitis, and ulcers. Reis

et al (87) reported that smoking has been linked to decreased mucus and bicarbonate secretion, thereby increasing the risk of ulcer formation. Nicotine, among other components in tobacco, has been found to have an adverse effect on the protective mucus of the gastric epithelium by altering bicarbonate. Similarly, coffee, including decaffeinated coffee, has been shown to increase stomach acid production and cause irritation to the stomach lining. These findings are supported by numerous studies in the surgical literature (88, 89).

7. Conclusion

H. pylori infection may also be an important cause of gastritis; therefore, H. pylori should be tested in patients with gastritis who have a complaint, and this bacterium should be used in the treatment of gastritis. Chronic gastritis should be diagnosed before it progresses and causes fatal diseases such as peptic ulcer or cancer, and it should be treated with both a healthy diet and appropriate medications. A personalized nutrition plan should be developed based on individual variations and symptoms, while considering any potential complications.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors have no conflicts of interest to declare regarding the publication of this article.

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