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Is There an Association between Oral Helicobacter pylori and Hypertension, Coronary Artery Disease?

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Abstract

Half of humanity harbors helicobacter pylori (*H. pylori*) in their stomach [1]. In addition to commonly causing peptic ulcer and gastritis, *H. pylori* is a major contributor for causing gastric cancer, worldwide the second most common cancer [2]. Gastric cancer patients are at least 80% sero positive for anti- *H. pylori* antibodies and gastric colonization is a well recognized cause of gastric lymphoma [1]. Despite discovery of a gastric etiological basis for *H. pylori*, there is a secondary issue that should be address (a) Why is the recurrence rate, after the successful eradication of *H. pylori* in patient's stomach approximately 13% per year, and (b) Is oral *H. pylori* involved in the recurrence of gastric infection? The result of our research in oral *H. pylori* presents evidence supporting the oral cavity as a second colonized site for *H. pylori*, besides primarily residing in the stomach, which plays a significant role in *H. pylori* diagnosis, transmission, and treatment [3] as well as non-gut organs *H. pylori* infection.

There are several reports indicated non-gut organs have been harbored of *H. pylori,* such as vagina [4], nasopharyngeal sinus cavities [5], coronary plaque [6], otitis media [7] and breast [8] beside stomach. The present article was designed to discussion on association of *H. pylori* with coronary artery and hypertension diseases as well as how to diagnosis and treatments on *oral H. pylori* infection.

Association of *H. Pylori* with Hypertension

Arterial hypertension is a risk factor for atherosclerosis of whose pathogenesis is unknown but had been reported as associated with *H. pylori* infection. Growing evidence underscores the causative role of endothelial dysfunction with infection. A possible association between *H. pylori* infection and cardiovascular and autoimmune disorders has been found [9]. The release of cytotoxic substances either of *H. pylori* origin or produced by the host may represent mediators of autoimmune sequelae. Migneco et al. demonstrated a significant decrease in blood pressure values, in particular in diastolic blood pressure values, after *H. pylori* eradication in hypertensive patients [7]. They indicated a high prevalence of *H.pylori* virulence factor CagA (CagA) positivity was found in those patients. The association between cardiovascular disease and *H. pylori* infection seems pronounced only in CagA-positive patients [10,11]. The possible links between hypertensive disease and *H. pylori* infection may involve the activation of the cytokine cascade with the release of vasoactive substances from the primary site of infection, or molecular mimicry between the CagA antigens of *H. pylori* and some peptides expressed by endothelial cells and smooth muscle cells [11].

Vinutha Shankar et al. reported 40 patients with hypertension and 40 normal controls were included in their study. The presence of *H. pylori* was confirmed by serological evidence of *H. pylori* IgG antibodies as estimated by ELISA (> 40 EU/ml considered as positive). 18 subjects with hypertension and 9 controls were positive for *H. pylori* as per serological evidence. Chi square test revealed that the difference in the number of seropositive cases was statistically significant ($p < 0.05$). Thus in their study *H. pylori* infection had significant association with hypertension as compared to controls according author' version [10]. Inflammation has been implicated in the pathogenesis of atherosclerosis, and markers of inflammation, have been reported to be associated with the risk of atherosclerosis related cardiovascular disease. They demonstrated a clinically significant decrease in blood pressure values, in particular in diastolic blood pressure values, after *H. pylori* eradication in hypertensive patients. They postulated that the possible links between hypertensive disease and *H. pylori* infection may involve the activation of the cytokine cascade with the release of vasoactive substances from the primary site of infection, or molecular mimicry between the CagA antigens of *H. pylori* and some peptides expressed by endothelial cells and smooth muscle. There has been a significant increase in subjects with seropositivity to *H. pylori* in hypertension as compared to normal. The importance of this association of *H. pylori* infection with hypertension is highlighted by the possibility of an effective intervention against *H. pylori* infection as the organism can be not easily eradicated using simple & reliable drug regimen. For described reason [8-10], we postulate oral *H. pylori* involving hypertension diseases, since patient has oral *H. pylori* infection that may results that *H. pylori* can swim into artery system of oral cavity. Therefore we suggest to examine *H. pylori* of oral cavity that not depending the results of urea breath test (UBT C[13] or C[14]). UBT C[13] or C[14] is a gold standard for diagnosis of stomach *H. pylori*, but is not so for detection in the mouth. We found that UBT C[13] has color blind that see *H. pylori* in the stomach, but can't detecting *H. pylori* in oral cavity. In medical practice, patients with negative results in UBT C[13] suggest that their stomach infection of *H. pylori* is cured. In fact, patients can present negative UBT results and yet exhibit *H. pylori* infection due to oral infection. The clinical study provides evidence that *H. pylori* oral infection is nonetheless present. In Asia, more than 90% of the population suffered from oral *H. pylori* infection but had negative UBT results [11,12]. This study also showed that oral antigen screening test could identify individuals who have no risk for *H. pylori* gastric infection. It further identified persons with no symptoms but with antigenic evidence of possible oral *H. pylori* infection who are thus at risk for developing gastric and no-gut disease. This information was not provided by UBT methods

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[12], then the oral *H. pylori* infection exits without treatment that can develop gastric and hypertension diseases [3].

HPS Technology

In order to know and how to use *H. pylori* antigen test (HPS) to diagnosis of oral *H. pylori* in the patients with hypertension but no effective on drug therapy: In this case you may try find if patients may have oral *H .pylori* infection.

This test was specifically detected in saliva using a lateral flow immuno chromatographic test device. The device for *H. pylori* antigen detection in saliva was identical to the device used for oral urease detection. The HPS test for saliva employed monoclonal antibody that was developed against oral urease.

Test procedure

No food or drink was allowed one hour prior to the test. A swab was put under the tongue for at least one minute. The swab was swirled vigorously for 15 seconds in a buffer solution, then we expunged as much liquid as possible from the swab by pressing and rotating the fiber portion against the wall of the tube. Two to three drops of saliva/buffer mixture were added into the sample well. As the test kit begins to work, one will see a purple color move across the result window in the center of the test disk. The presence of two color bands ('T' band and 'C' band) within the result window indicates a positive result. The presence of only one purple color band indicates a negative result.

Specificity

An in-house study was conducted with three separate lots of the HPS test to determine its specificity. The following common oral bacteria had been applied:

Actinomyces naeslundii, Actinomyces odontolyticus, Bifidobacterium dentium, Corynebacterium matruchotii, Gemella haemolysans, Granulicatella adiacens, Streptococcus gordonii, S salivarius, S. sanguinis, and *Veillonella parvula.* All of the above were analyzed and did not show interference or cross-reactivity with the test.

Sensitivity

The test's sensitivity was 10 ng/ml HPS antigen [9].

Drug Regimen is not Effective for Eliminating Oral *H. pylori*

Drug treatment on stomach *H. pylori* infection has no effective in *H. pylori* infection of oral cavity. *H. pylori* exists in between the teeth and gums called "bio- film membrane" (Bifilm), also known as plaque barrier. It is resistance when the drug into this area. This is why conventional tratmentatment for *H. pylori* eradication *H. pylori* infection, but is not efficacy of oral *H. pylori* in dental plaque. Miyabayashi *etc.* [13] found the eradication success rate was significantly lower in the oral *H. pylori*-positive cases (12/23, 52.1%) than in the negative cases (22/24, 91.6%) at 4 weeks after the therapy (p = 0028). Two years later, only 16 of the 23 (69.5%) oral *H. pylori*-positive cases were disease-free, as compared to 23 of the 24 (95.8%) oral *H. pylori*-negative cases (p = 018). They concluded *H. pylori* in the oral cavity affected the outcome of eradication therapy and was associated with a recurrence of gastric infection and recommend that oral *H. pylori* should be examined by nested PCR and, if positive, should be considered a causal factor in refractory or recurrent cases. Our study show the efficacy rate of treatment on stomach *H. pylori* infection at 82.26% for patients received treatment of mouthwash combined with drug eradication; but only at 61.33% efficacy when patients received drug eradication on stomach. So treatment of oral cavity *H. pylori* raise about 20% efficacy when combined treatments of both mouth and stomach [12-15].

Non-antibiotic Formula

There is non-antibiotic treatment for oral *H. pylori* infection

available. Our studies [3,12] indicated e-polylysine (L) and the Glycerol Monolaurate (GM) used in mouth washing solution for eliminating oral H. pylori. The L is typically produced as a homo-polypeptide of approximately 25-30 L-lysine residues. The epsilon (e) refers to the linkage of the lysine molecules. In contrast to a normal peptide bond that is linked by an alpha carbon group, the lysine amino acids are molecularly linked by the epsilon amino group and the carboxyl group. L belongs to the group of cationic polymers. In water, L contains a positively charged hydrophilic amino group. It is adsorbed electro statically to the cell surface of the bacteria, followed by a stripping of the outer membrane. This eventually leads to the abnormal distribution of the cytoplasm, causing damage to the *H. pylori* cell. GM is the mono-ester formed from glycerol and lauric acid. *H. pylori* is extremely sensitive to GM, however there are no reports of L or GM killing *H. pylori in vivo.* Since both have had a safe record in the food industry, we use L-GM successfully eliminate *H.* pylori of oral cavity within 2 to 3 months. In China alone, more than 280 million people carry oral *H. pylori,* which results in 28 million recurrences of stomach *H. pylori* infection and the abuse of antibiotics by over use [16] because oral *H. pylori* had been missing diagnoses and recurrent stomach *H. pylori* infection.

Is there an Association of *H. Pylori* with Coronary Heart Disease?

Mehran et al. reported that *H. pylori* infection is one of the probable risk factors for coronary heart disease independent of history of diabetes mellitus, dyslipidemia, hypertension, C-reactive protein. Their findings showed patients with *H. pylori* infection are about 3 times more at risk of coronary heart independent of disease history of diabetes mellitus, dyslipidemia, hypertension, C-reactive protein [17]. Accordingly *H. pylori* association with some cardiovascular risk factors has been suggested and also it was shown that this bacterium induces some inflammatory cytokines. In their study, the role of these risk factors and cytokines were adjusted, therefore, the remained higher chance may be due this adjusting and reveal the independent role of *H. pylori* infection in atherosclerosis process. Since they found *H. pylori* DNA has been documented in coronary plaque [18] that is most important evidence indicated link between *H. pylori* and coronary disease. Of course the way of developing process of coronary disease needs further investigation. But the significant pathogenic links *H. pylori* to coronary artery lumen narrowing are present [19]. Also eradication therapy on stomach *H. pylori* infection has prognosis improving effects in coronary artery disease had been reported [18].

They proposed the *H. pylori* infection how to developing coronary heart are as follows process; Firstly, damaging influence of *H. pylori* and its products like cytokines, cytotoxins on coronary endothelium; secondly, activation of immune mechanisms by this bacteria which react with the nuclei of monocytes in atherosclerotic vessel wall and cytoplasm of fibroblast-like cell in atherosclerosis plaques; thirdly, *H. pylori* induces releasing nitric oxide by vascular endothelium interferes with fibrinogen level which cause the reduction of the normal capacity of muscular relaxation and lead to vasoconstriction and adverse hemodynamic balance; finally, this infection elevates thromboxane which is measured as TXB that results in platelets activation [17].

Mayr et al. reported infections with virulent CagA-bearing *H pylori* strains may contribute to the pathogenesis of early atherosclerosis by aggravating immune-inflammatory reactions [19]. Again, Cag A is the most toxic strains resulting stomach cancer and commonly found in oral cavity [3].

Kowalski et al. proposed the role of inflammation in the pathogenesis and progression of coronary artery [18], but it still remains unclear. how inflammatory changes in the vessel wall by *H. pylori.*

The prevalent condition and the exact mechanism of initiation of atherosclerotic vascular disease also remain unclear. Although the sero epidemiological and eradication studies have suggested a causal

relationship between *H. pylori* infection and coronary heart disease; the issue is still controversial.

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