E. Why *H. pylori* of Oral Cavity Effective Rate on Eradication of Stomach *H. pylori* Therapy?

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Published Date: December 22, 2016

If there were no living *H. pylori* exists in the oral cavity and all *H. pylori* detected by PCR were reflux from the stomach that was thought to survive in the oral cavity for only a few hours. Then dead *H. pylori* should not have any negative effect on the drug eradication of *H. pylori* infections of the stomach. However we found a different fact that treatment of the oral infection increased the success rate of eradication of the stomach infection from 61.33% to 82.26% in the 95% CI ranges. From results, we concluded that the successful rate of eradication of gastric *H. pylori* bears a significant relationship to the oral infection from *H. pylori* [1]. Our finding explaining why the annual *H. pylori* recurrence rates were 13.2 % and second-year and the third-year follow-up, were 18.4 % third year, 20 % [2]. In developed countries, the recurrence rates *H. pylori* after successful eradication were very low. The discrepancy exists and determining by economic status.

THE CLOSE RELATIONSHIP BETWEEN PERIODONTAL HEALTH AND *H. PYLORI* INFECTION

Dye BA et al. report that a total of 4504 participants who completed a periodontal examination and tested positive for *H. pylori* antibodies that show periodontal pockets with a depth of 5 mm or more were associated with increased odds of *H. pylori* seropositivity (odds ratio [OR]=1.47; 95% confidence interval [CI]=1.12,1.94). The conclusion was that poor periodontal health, which is characterized by advanced periodontal pockets, could be associated with *H. pylori* infection in adults [3]. Fernández-Tilapa G et al. found that the prevalence of *H. pylori* in the oral cavity was higher among seropositive subjects than sero negative ones [4]. Furthermore, Nisha KJ et al. reported that there is a highly significant association between periodontal disease and the colonization of *H. pylori* in dental plaque [5]. Tsami A et al. detected *H. pylori* in sub gingival dental plaque of children and their family [6].

Several reports have indicated that *H. pylori* colonies could be grown only from root canals but not from plaque. The root canals of endodontic-infected teeth could be a reservoir for live *H. pylori* that could serve as a potential source of transmission [7,8].

WHY WOULD THE TRADITIONAL TREATMENT OF GASTRIC INFECTION BE INEFFECTIVE AGAINST ORAL INFECTION?

Drug treatment on stomach *H. pylori* infection has no effective in *H. pylori* infection of oral cavity. *H. pylori* exist 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 treatment for *H. pylori* eradication *H. pylori* infection, but is not efficacy of oral *H. pylori* in dental plaque. Miyabayashi etc. [9] 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.

THE PROGRESSIVE LOSS OF EFFICACY OF STANDARD ERADICATION THERAPIES HAS MADE THE TREATMENT OF *H. PYLORI* MORE CHALLENGING THAN EVER

Endoscopic-guided antibiotic susceptibility testing had previously been suggested to guide treatment after failure of second-line therapies. However, its role has expanded over the years, in accordance with the current Maastricht Guidelines. Several authors have dealt with this topic, developing both efficacy trials and cost-effectiveness trials against resistant *H. pylori* infections as

well as infections in patients. However, results are not homogeneous enough to provide definite advice, because antibiotic resistance is not the only reason for treatment failure. Moreover, the culture-guided approach is surrounded by many practical issues, such as the availability of both endoscopy units and microbiology laboratories, and the need for a standard of quality that cannot be satisfied everywhere [10]. We proposed the key conception that *H. pylori* has second colonized site in oral cavity beside of stomach. However, some authors have drawn premature conclusions that "oral *H. pylori* cannot be cultured" and "the oral cavity is not a colonized site", which has become the main theoretical basis to oppose oral *H. pylori* colonization. Because the majority of physicians and scientists in this field ignore the colonized cavities of H. pylori, approximately 20% of the population of Asia suffers from oral *H. pylori* infection. 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 overuse [11]. The massive antibiotic pollution that appears in food, water, and children's urine has become a serious concern worldwide [12]. Antibiotic abuse kills 80,000 Chinese people every year and leads to extra medical spending of 11.7 billion dollars across the country, which could become a global problem.

IS UREA BREATH TEST A GOLD STANDARD FOR DIAGNOSIS OF *H. PYLORI* INFECTION?

The Urea Breath Test **(UBT)** C13, 14 is a good rapid diagnostic procedure used to identify stomach infections by H. pylori. It is based upon the ability of *H. pylori* to convert urea to ammonia and carbon dioxide. Urea breath tests are recommended in leading society guidelines as a preferred non-invasive choice for detecting *H. pylori* of stomach before and after treatment with diagnostic efficacy at 96.7% sensitivity and 96.2% specificity. However UBT is not a test for detection *H. pylori* in the mouth. We found that UBT C13 can't detect *H. pylori* in oral cavity as a person has dysfunction of color blind that can't see well for certain color. In medical practice, patients with negative results in UBT C13 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 20-30 % of the population suffered from oral *H. pylori* infection but had negative UBT results [13]. This study also showed that oral antigen screening test **(HPS)** could identify individuals who have no risk for *H. pylori* gastric but oral 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 disease. This information was not provided by UBT methods.

WHAT IS THE GOOD TEST FOR DETECTING *H. PYLORI* OF ORAL CAVITY IN CLINICAL SETTINGS?

PCR is a high sensitivity test for oral *H. pylori*, but it is not convenient in clinical settings. So, first a high sensitivity and specificity test in saliva should be established. Then we will have a much easier time of running clinical trial on a large number of patients to obtain a greater number of data, to find the positive correlation between oral and stomach *H. pylori* infection.

The most common bacteria causing infection across the world is *H. pylori*, which colonizes the human stomach. This bacterium has also been detected in some extra-gastric ecological niches such as the oral cavity and water. However, the results of *H. pylori* detection in extra-gastric ecological niches are controversial. The UBT cannot detect *H. pylori* in the oral cavity. The improvement of the sensitivity and the specificity of the detection methods appear to be some of the main bottleneck issues in providing compelling evidence [14,15].

HPS (*H. pylori* antigen test for oral urease): It was specifically detected in saliva using a lateral flow immune 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, and 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 [13]. Our studies show that in 20-25% of UBT negative individual have positive of HPS test that indicated *H. pylori* exists in oral cavity when stomach no infection.

NON ANTIBIOTIC TREATMENT FOR ELIMINATING ORAL *H. PYLORI*

There is non-antibiotic treatment for oral *H. pylori* infection available. Our studies indicated e-polylysine (L) and the Glycerol Monolaurate **(GM)** used in mouth washing solution. 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. 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 [1]. See Figure 1.

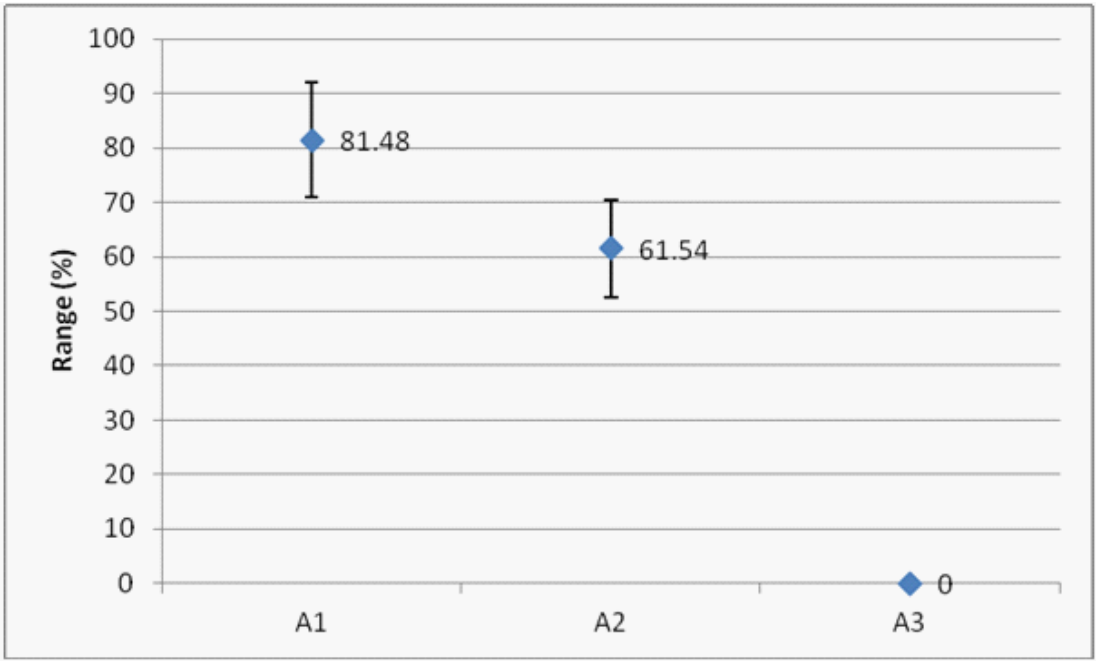

Figure 1: Success Rate of Treatment on Stomach Infection of A group as determined by negative of UBT C^{13}.

A1: patients had been received L-GM treatment on oral cavity for two months and combined with regula eradication on stomach *H. pylori* infection.

A2: Patients received regular eradication on stomach *H. pylori* infection.

A3: No treatments provided.

CONCLUSION

1. A colonized site of *H. pylori* can exist in the oral cavity.

2. In medical practice, it is assumed that patients with negative UBT results are cured of their stomach *H. pylori* infection, but in fact, patients can present negative UBT results and exhibit oral H. pylori. This information was not provided by UBT methods.

1. If there is a live *H. pylori* colony in the oral cavity, then it would have a negative influence on the eradication of a stomach infection. In the classic *H. pylori* eradication programs, there are no clear measures of oral H. pylori; frequent relapses become more critical.

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