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Annals of Clinical Cytology and Pathology

Opinion

Is Urea Breath Test a Gold Standard for Diagnosis of *H. pylori* Infection?

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Submitted: 09 March 2016
Accepted: 21 March 2016
Published: 04 April 2016

The urea breath test UBT C[13,14] 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 C[13] can't detecting *H. pylori* in oral cavity such 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 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 20-30 % of the population suffered from oral *H. pylori* infection but had negative UBT results [1]. 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.

The principle of UBT test; patients swallow urea labeled with an uncommon isotope, either radioactive carbon-14 or non-radioactive carbon-13. In the subsequent 10–30 minutes, the detection of isotope-labelled carbon dioxide in exhaled breath indicates that the urea was split; this indicates that urease (the enzyme that *H. pylori* uses to metabolize urea) is present in the stomach, and hence that *H. pylori* bacteria are present. In UBT test, since the urea labeled is not dissolved in the mouth, so there were no isotope-labeled carbon dioxide in exhaled breath that is why UBT can't provide information of *H. pylori* in the oral cavity. Secondly, the principle of UBT test based on the theory of stomach harbors *H. pylori* instead oral cavity. Over the past twenty years, the existence of oral *H. pylori* infection has been controversial, without a definite conclusion. It was proposed that no living *H. pylori* exists in the oral cavity and that the positive results detected by PCR from oral samples indicate that the presence of *H. pylori* fragments, rather than living bacteria, or are due to reflux from the stomach, which is infected with *H. pylori* could not be cultivated from PCR-positive samples. The *H. pylori* originating from stomach reflux was thought to survive in the oral cavity for only a few hours because of the high oxygen concentration of the mouth. If the above-proposed idea is correct, then the fragmented or dead *H. pylori* should not have any negative effect on the drug eradication of *H. pylori* infections of the stomach [1,2]. However, the proposed idea contradicts with PCR studies [3,4] the fact of oral hypoxia environment [5,6] eradication can't eliminate Oral *H. pylori* infection [7,8] *H. pylori* can be cultured in the oral cavity [9], the same original source of Oral and Stomach *H. pylori* [10,11]. Lower rate of eradication on stomach *H. pylori* when oral *H. pylori* positive [12] and Meta analysis [13,14].

Therefore, we proposal a new view that indicated *H. pylori* colonization of the oral cavity. Before we discussion on *H. pylori* colonization of the oral cavity, I like introduce *H. pylori a*ntigen test for oral urease (HPS) technology that can detecting *H. pylori* of the oral cavity first.

HPS Technology

HPS (*H. pylori a*ntigen test for oral urease): It was specifically detected in saliva using a lateral flow immunochromatographic test device. The device for *H. pylori* antigen detection in saliva was identical to the device used for oral urease detection in which has same principle of UBT. 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 mg/ml HPS antigen [15]. 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 [9,15].

Because the majority of physicians and scientists in this field ignore the colonized cavities of *H. pylori,* approximately 20-30 % 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 [16]. The massive antibiotic pollution that appears in food, water, and children's urine has become a serious concern worldwide [17]. 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.

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* 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.* [12] 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 [10].

Non-antibiotic Formula

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 (Figure 1).

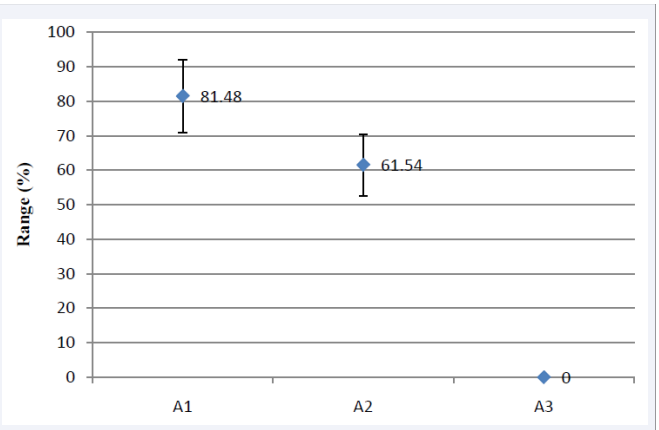

Figure 1 Effective on Stomach Infection. Success Rate of Treatment on Stomach Infection of A group as determined by negative of UBT C^{13}.
A1: patients had been received L-GM treatment on oral cavity for two months and combined with regular eradication on stomach *H. pylori* infection.
A2: Patients received regular eradication on stomach *H. pylori* infection.
A3: No treatments provided.

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Cite this article

Wang XM, Yee JKC (2016) Is Urea Breath Test a Gold Standard for Diagnosis of H. pylori Infection?. Ann Clin Cytol Pathol 2(1): 1018.