

## What is the effect of radioiodine therapy on *Helicobacter pylori* infection?

Celil Alper USLUOĞULLARI<sup>1\*</sup>, Eda DEMİR ÖNAL<sup>1</sup>, Elif ÖZDEMİR<sup>2</sup>, Sedat CANER<sup>1</sup>,  
Osman ERSOY<sup>3</sup>, Reyhan ERSOY<sup>4</sup>, Bekir ÇAKIR<sup>4</sup>

<sup>1</sup>Department of Endocrinology and Metabolism, Atatürk Teaching and Research Hospital, Ankara, Turkey

<sup>2</sup>Department of Nuclear Medicine, Atatürk Teaching and Research Hospital, Ankara, Turkey

<sup>3</sup>Department of Gastroenterology, Faculty of Medicine, Yıldırım Beyazıt University, Ankara, Turkey

<sup>4</sup>Department of Endocrinology and Metabolism, Faculty of Medicine, Yıldırım Beyazıt University, Ankara, Turkey

Received: 30.01.2013 • Accepted: 01.08.2013 • Published Online: 31.03.2014 • Printed: 30.04.2014

**Background/aim:** *Helicobacter pylori* is an important human pathogen associated with gastric and duodenal ulcers, gastric mucosa-associated lymphoid tissue lymphoma, and adenocarcinoma. Radioiodine (RAI) treatment plays an important role in the management of differentiated thyroid cancer and primary hyperthyroidism. It is known that during RAI treatment, a considerable amount is absorbed by the stomach as well. In this study we aimed to reveal any therapeutic impact of RAI on *H. pylori* infections.

**Materials and methods:** Eighty-seven patients who were hospitalized for RAI treatment were consecutively included in this study. Of those, 76 patients had differentiated thyroid cancer and 11 had primary hyperthyroidism. The urea breath test (UBT) was performed on the day before RAI, and the test was repeated after 2 months.

**Results:** The dose of RAI was  $115 \pm 3.3$  mCi (range: 100–150 mCi) in the patients with malignant disease and  $22.7 \pm 1.4$  mCi (range: 20–30 mCi) in the remaining patients. Among the patients with differentiated thyroid cancer, 44 (57%) had positive and 32 (43%) had negative UBT tests prior to RAI. Four (36%) patients with hyperthyroidism had pretreatment positive UBT tests and 7 (64%) had negative tests. The results of UBT conducted 2 months after RAI therapy were identical in every patient, which means that none of the patients with positive UBT became UBT-negative ( $P = 1$ ).

**Conclusion:** RAI does not have any therapeutic effect on *H. pylori* infection.

**Key words:** *Helicobacter pylori*, radioiodine therapy, differentiated thyroid cancer, urea breath test

### 1. Introduction

*Helicobacter pylori* is a gram-negative, spiral-shaped, pathogenic bacterium that specifically colonizes the gastric epithelium (1). The ultimate clinical manifestations of *H. pylori* infection include gastric and duodenal ulcers, gastric mucosa-associated lymphoid tissue lymphoma, and adenocarcinoma, but most infected individuals remain asymptomatic for life despite developing chronic histologic gastritis (1–3). Because there is currently no *H. pylori*-specific antibiotic available to cure infections, treatment requires combining several medications. On the other hand, during the last 2 decades, the widespread use of certain antibiotics in the general population has increased the occurrence of *H. pylori* resistance in different countries, and *H. pylori* antibiotic resistance has become a major factor leading to eradication failure (4).

Radioiodine (RAI) treatment plays an important role in the management of differentiated thyroid cancer

(DTC). RAI destroys any residual microscopic thyroid carcinoma. It also facilitates follow-up and early detection of recurrent or metastatic disease by measurement of serum thyroglobulin (5). Isotope therapy is one of the methods also used in treating primary hyperthyroidism. Indications for RAI therapy in Graves–Basedow disease include recurrent hyperthyroidism after thyrostatic treatment or thyroidectomy and side effects observed during thyrostatic treatment. In toxic nodules, isotope therapy is the first choice of therapies (6).

During isotope treatment, RAI is distributed throughout the normal tissues, which possess sodium/iodine (Na/I) symporters, as well as malignant tissues, and a considerable amount is absorbed by the stomach (7,8). On the basis of this observation, a group of researchers previously questioned whether the effect of the high radiation induced by RAI in the stomach is effective in the eradication of *H. pylori* infections, and they showed a

\* Correspondence: calperuslu@yahoo.com

suppressive effect (9). In this study we aimed to reveal any therapeutic impact of RAI on *H. pylori* infection.

## 2. Materials and methods

Eighty-seven patients who were hospitalized in our Nuclear Medicine Department for RAI treatment were consecutively included in this study between January 2011 and January 2012. Exclusion criteria included previous eradication therapy or use of bismuth compounds, antibiotics, and antisecretory drugs within the last 2 months. Females who might be pregnant (as a contraindication for RAI therapy) and patients with hepatobiliary, pulmonary, or metabolic diseases; previous gastric surgery; or dyspepsia were also excluded. The Ankara Atatürk Education and Research Hospital Ethics Committee for Human Studies approved the protocol, and all participants provided informed consent. The urea breath test (UBT) was performed for all patients on the day before RAI therapy. The UBT was repeated 2 months after RAI administration, a period during which patients were advised not to consume bismuth compounds, antibiotics, or antisecretory drugs.

During the urea breath test, patients swallowed 37 kBq (1  $\mu$ Ci) of an encapsulated form of  $^{14}$ C-urea/citric acid (Helica Noster System, Stockholm, Sweden) in 25 mL of water after overnight fasting. Breath samples were collected with a special dry cartridge system (Heliprobe BreathCard; Noster System) after 10 min. Patients exhaled gently into the cartridge mouthpiece until the indicator membrane changed color from orange to yellow. The BreathCard was inserted into a special small desktop Geiger-Müller counter (Heliprobe Analyzer; Noster System), and activity was counted for 250 s. Results were expressed both as counts per min (cpm) and as grade (0: not infected, <25 cpm; 1: equivocal, 25–50 cpm; 2: infected, >50 cpm), as suggested by the manufacturer according to the counts obtained from the cartridges.

Descriptive statistics were generated for all study variables, including mean and standard deviation for continuous variables and relative frequencies for categorical

variables. Relations between subgroups were analyzed by using the chi-square test for categorical variables and the t-test for continuous variables. One-sided values of  $P < 0.05$  were considered statistically significant. SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

## 3. Results

Of the 87 patients who underwent RAI treatment, 76 had DTC and 11 patients had hyperthyroidism. The dose of RAI was  $115 \pm 3.3$  mCi (range: 100–150 mCi) in the patients with malignant disease and  $22.7 \pm 1.4$  mCi (range: 20–30 mCi) in the remaining patients. Among the patients with DTC, 44 (57%) had positive and 32 (43%) had negative UBT tests prior to RAI. Four (36%) patients with hyperthyroidism had pretreatment positive UBTs and 7 (64%) had negative tests. The results of UBT 2 months after RAI therapy were identical in every patient, which means that none of the patients with positive UBT became UBT-negative ( $P = 1$ , Table).

## 4. Discussion

*H. pylori* eradication failure is an important problem. The main reasons for eradication failure are antibiotic resistance, poor compliance with antibiotic regimens, and rapid metabolism of proton pump inhibitors (PPI) (10). Triple treatment, including PPI-clarithromycin and amoxicillin or metronidazole, was once the first-line treatment throughout the world (11). However, this combination has lost some efficacy and often leads to the cure of only 70% of the patients (10). The background rate of clarithromycin resistance is critically important because it is associated with the failure of standard triple therapy (12). For this reason, bismuth-containing quadruple therapies are recommended for first-line empirical treatments in areas of high clarithromycin resistance (>15%–20%), according to the Maastricht IV consensus report (13). If this regimen is not available, sequential treatment or a nonbismuth quadruple therapy is recommended.

**Table.** The results of urea breath tests (UBTs) in patients admitted for radioiodine (RAI) treatment.

	UBT after RAI therapy		Total
	Positive	Negative	
UBT before RAI therapy			
Positive	46	-	46
Negative	-	39	39
Total	46	39	85

The antibiotic treatment of *H. pylori* infections carries some risk. Patients frequently experience side effects, which include metallic taste in the mouth, flushing, headache, nausea, vomiting, diarrhea, constipation, and stomach cramps (2,14). Antibiotics can enable the overgrowth of *Candida albicans*, which can result in vaginitis or other complaints. In addition, antibiotic therapy can be complicated by the development of pseudomembranous colitis. Moreover, antibiotic treatment could lead to the overgrowth of antibiotic-resistant strains of *H. pylori*. For these reasons, the search continues for alternatives to the conventional triple therapy treatment for *H. pylori* infections.

At present, the most promising natural treatment is a mixture of black currant seed oil and fish oil. A study showed that this mixture can eradicate *H. pylori* in 20% of cases (15). In addition, certain probiotics and prebiotics had efficacy as an adjuvant treatment in reducing side effects, and, in this way, they may indirectly improve the therapeutic success (16). Mastic gum has been shown to promote the healing of duodenal ulcers in vitro (17). Vitamin C and berberine suppress *H. pylori* temporarily in some patients (18,19). To date, none of the alternative therapies, however, have clear-cut scientific evidence to be acceptable alternatives to conventional antibiotic regimens (20).

RAI is widely used in the treatment of DTC and, to a lesser extent, in hyperthyroidism. Following RAI therapy, a considerable amount of the extrathyroidal iodide (15%) is located in the stomach (21). The residence time of radioactive iodine in the stomach is  $1.23 \pm 0.31$  h (0.84–1.62 h) in the euthyroid state and  $0.9 \pm 0.08$  h (0.82–1.04 h) in the hyperthyroid state, which may be long enough to have marked biologic or therapeutic effects (21). Although RAI therapy is not a logical method for treatment in patients suffering from *H. pylori*, it can be potentially used in the food industry to sterilize food. Based on these facts, Gholamrezanezhad et al. investigated

whether the high radiation induced by RAI in the stomach is effective in the eradication of *H. pylori* infections (22). They showed a significant reduction in the number of positive UBT results in a group of patients with DTC who underwent RAI treatment (32.4% of UBT-positive cases became UBT-negative). The authors concluded that their findings provided an indirect piece of evidence about the radiosensitivity of the bacteria and could have future clinical applications (22). Our findings, which show identical UBT results despite RAI administration, do not support the conclusion of the study by Gholamrezanezhad et al. Our search in the scientific banks of MEDLINE and EMBASE found no trials evaluating the beneficial effects of RAI therapy on any infectious disorders, including *H. pylori*, except for the above-mentioned series (22). There was also no hypothesis regarding the mechanism of the possible therapeutic effect of RAI on *H. pylori*. The authors speculated that RAI causes intermittent gastritis with the subsequent reduction of acid secretion and, therefore, reduced sensitivity of the UBT. Hence, they suggested that radioactive iodine might have suppressed the *H. pylori* infection and made the results of the UBT false negative (22). We disagree with the authors because if this hypothesis were true, we would have seen at least one case of a negative UBT after RAI in our series. In order to rule out the possibility of a false negative UBT, an ideal study would include a second diagnostic method for *H. pylori*. We think that the main reason for the post-RAI therapy negative UBTs in this series may be noncompliance with the antibiotic and PPI-free period. Our studies also showed that the dose of RAI has no association with *H. pylori* eradication, as no single UBT became negative after high or low doses of RAI.

In conclusion, our study revealed that RAI does not have any therapeutic effect on *H. pylori* infection. Future studies of this topic should involve animal subjects and a second diagnostic method for *H. pylori*, ideally histology.

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