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The Effect of ^{131}I Therapy on the Eradication of *Helicobacter pylori* in Patients with Thyroid Disorders: A Preliminary Study

Farhad Pourfarzi[1], Hossein Pakrouy[2], Ali Mohammadian Erdi[3], and Elnaz Faghfuri[1]

[1]*Digestive Disease Research Center, Ardabil University of Medical Sciences, Ardabil, Iran;* [2]*Ardabil Nuclear Medicine Center, Ardabil University of Medical Sciences, Ardabil, Iran; and* [3]*Department of Anesthesiology, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran*

The leading cause of gastritis and its complications is *Helicobacter pylori*. Radioactive iodine (^{131}I) accumulates significantly in the stomach after consumption. On this basis, we decided to determine whether different doses of ^{131}I in the stomach would be effective in eradicating the infection. **Methods:** All patients with hyperthyroidism or differentiated thyroid carcinoma who were referred for ^{131}I treatment were invited to the study. A stool antigen test was conducted before consumption of ^{131}I (0.15–5.5 GBq) and was repeated 2 mo later to detect *H. pylori* infection. **Results:** *H. pylori* positivity was found in 51.8% (14/27) of the patients. At 2 mo after treatment, 13 of the 14 patients with differentiated thyroid carcinoma or hyperthyroidism who had been identified as positive for *H. pylori* stool antigen before ^{131}I administration were still positive, representing a nonsignificant eradication rate of 7.1%. **Conclusion:** Administration of ^{131}I to patients with *H. pylori* did not show potential to eliminate the infection.

Key Words: *Helicobacter pylori*; ^{131}I; differentiated thyroid carcinoma; hyperthyroidism

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The leading cause of chronic gastritis, peptic ulcer, gastric mucosa–associated lymphoid tissue lymphoma, and gastric cancer is *Helicobacter pylori,* a gram-negative bacteria that infects the human gastric mucosa (*1*). It has recently been proposed that *H. pylori* may be related to extraintestinal disorders such as vitamin B_{12} deficiency, iron-refractory iron-deficiency anemia, and immune thrombocytopenic purpura (*2*). Worldwide, *H. pylori* has been considered a group I carcinogen (*3*), and its eradication leads to healing of peptic ulcers, preventing their recurrence and reducing the risk of gastric cancer (*4*). In addition, *H. pylori*–related diseases, including mucosa-associated lymphoid tissue lymphoma, atrophic gastritis, and intestinal dysplasia, are also curable after antibiotic therapy (*5*).

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For correspondence or reprints, contact Elnaz Faghfuri (elnaz.faghfuri@gmail.com).
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A triple-therapy regimen comprising a proton pump inhibitor and 2 antimicrobial agents such as amoxicillin, clarithromycin, metronidazole, levofloxacin, and tetracycline is commonly used for eradication. However, the success rate of eradication therapy is dependent on many factors, such as smoking habits and patient compliance. The main factor in reducing therapy efficacy is antibiotic resistance (*6*). Antibiotic resistance is greater in developing countries than in developed countries (*7*). Moreover, the frequency of antibiotic use is often a factor in the rate of antibiotic resistance (*8*). Considering the decrease in the effectiveness of antibiotics against *H. pylori* strains, the risks caused by antibiotic use, and the need to prevent complications and deaths caused by it, a new therapeutic approach is required.

Remarkably, the stomach and thyroid have a valuable ability to concentrate iodide (*9*). Thyroid cells phylogenetically originate from iodine-concentrating primary digestive cells. In evolution, these cells move and become specialized in absorbing and storing iodine. Whole-body scans of cancer patients who received high doses of ^{131}I have indicated evidence of ^{131}I uptake in malignant tissue, normal thyroid tissue, the gastric wall, and the salivary glands (*10*). Gholamrezanezhad et al. (*11*) showed that radioactive iodine (^{131}I) therapy in patients with differentiated thyroid carcinoma (DTC) and a positive pretreatment urea breath test (UBT) correlated with a significant decrease in the UBT-positive rate. Despite these authors' acknowledgment that ^{131}I would not be a reasonable therapy for the typical patient with *H. pylori,* these results could be applied to the use of ^{131}I in eliminating *H. pylori* in the clinical setting and the food industry. Ionizing radiation directly disturbs the structure of DNA by causing DNA breaks. Secondary effects are the production of reactive oxygen species that oxidize proteins and lipids and cause multiple DNA damages (*12*). Considering that our geographic region (Ardabil, Iran) has a high prevalence of *H. pylori* infection, we felt prompted to determine whether different doses of ^{131}I in the stomach are effective in eradicating this infection.

MATERIALS AND METHODS

Patient Selection

The study design was approved by the Ethics Committee of Ardabil University of Medical Sciences. Patients with

TABLE 1
Clinical and Therapeutic Details of 18 Patients with DTC or Hyperthyroidism and *H. pylori* Infection Treated with ^{131}I

Patient no.	Age (y)	Sex	Diagnosis	Treatment dose (GBq)	Hp stool Ag before ^{131}I	Hp stool Ag after ^{131}I
1	58	M	HT	0.74	Positive	Positive
2	44	F	PTC	0.15	Positive	Positive
3	60	F	PTC	0.2	Positive	Positive
4	36	F	PTC	0.2	Positive	Positive
5	61	M	PTC	5.5	Positive	Positive
6	50	F	PTC	5.5	Positive	Positive
7	38	F	PTC	5.5	Positive	Positive
8	43	F	PTC	3.7	Positive	Positive
9	43	M	HT	1.1	Positive	Positive
10	43	F	PTC	5.5	Positive	Positive
11	31	F	PTC	0.2	Positive	Positive
12	33	F	PTC	5.5	Positive	Positive
13	50	F	PTC	3.7	Positive	Positive
14	41	F	PTC	5.5	Positive	Negative

Hp = *H. pylori*; Ag = antigen; HT = hyperthyroidism; PTC = papillary thyroid carcinoma.

DTC or hyperthyroidism who had been referred to the Ardabil Nuclear Medicine Center for ^{131}I therapy were asked to participate. Informed consent was obtained from the participants before the research began.

The exclusion criteria comprised previous attempts to eradicate *H. pylori* using antibiotics or antacids in the previous 1 mo or bismuth in the previous 3 mo, a history of gastrectomy, and pregnancy or lactation.

To evaluate the response to a standard treatment protocol, our research restricted data analysis to patients with DTC or hyperthyroidism who had never previously taken ^{131}I.

Experimental Design

Before therapy, all patients were asked to provide stool samples for *H. pylori* antigen testing. Stool samples were kept at −20°C until testing. Only patients who were treated with ^{131}I and had a positive *H. pylori* stool antigen test were eligible for the study. ^{131}I in the range of 0.15–5.5 GBq was administered to patients with DTC or hyperthyroidism. Subsequently, these patients were told not to use any antibiotics, antacids, or bismuth and to return for stool sample testing 8 wk after treatment.

H. pylori Antigen Test

We used a qualitative and immunochromatographic assay to detect *H. pylori* antigens in stool samples. Each sample was placed into a well and allowed to react with particles coated with anti–*H. pylori* antibodies. The mixture then moved toward the membrane by capillary action. If *H. pylori* antigens were present at detectable levels in the sample, a visible colored signal was produced. The appearance of a colored band at the result line and at the control line was considered positive. Complete absence of the control band was considered invalid, regardless of the appearance of the result line (*13*).

Statistical Analysis

Because of the dichotomous nature of all dependent variables (positive/negative), the McNemar test with the exact method was used to determine any differences before and after the interventions. A P value of 0.05 indicated a statistically significant difference for all compared variables. Statistical analysis was done using SPSS software version 26.0 (IBM).

RESULTS

The ratio of desired changes to undesired changes was 1 to 13 ($P = 1$). All 14 patients positive for *H. pylori* antigen had a repeat stool antigen test for the presence of *H. pylori* 8 wk after ^{131}I therapy. None of the patients had used antibiotics, antacids, or bismuth during the intervention period. *H. pylori* positivity was seen in 92.8% (13/14) of the patients (Table 1). Different doses (0.15–5.5 GBq) had no significant effect on *H. pylori* eradication. Of the 14 subjects studied, one (a 41-y-old woman with DTC who received a dose of 5.5 GBq) became negative 2 mo after treatment (Table 1).

DISCUSSION

The prevalence of *H. pylori* in eastern and southern Europe, South America, and Asia is often higher than 50%, and most infected people are asymptomatic. Currently, a proton pump inhibitor combined with antibiotic therapy is suggested for patients with active *H. pylori* infection. In the study of Gholamrezanezhad et al. (*11*), on 71 patients with DTC and a positive pretreatment UBT result, ^{131}I therapy at a dose of 3.7–7.4 GBq was related to a significant decrease in UBT positivity: 32.4% of UBT-positive patients became negative after 2 mo of treatment. These findings provide indirect evidence of *H. pylori* susceptibility to ^{131}I treatment. In another study, by Xu et al., the mean amount of

TABLE 2
Comparison of Present Findings with Previous Findings on ^{131}I Effect on *H. pylori* Eradication

Hp-positive patients before ^{131}I therapy (*n*)	^{131}I therapy dose (GBq)	Hp-negative patients after ^{131}I therapy (*n*)	Test used to evaluate Hp infection	Reference
14 with HT or PTC	0.15–5.5	1	SAT	Present study
71 with DTC	3.7–7.4	23	UBT	(*11*)
42 with DTC	NA	5	UBT	(*14*)
18 with DTC	3.7–7.4	0	SAT	(*17*)

Hp = *H. pylori*; HT = hyperthyroidism; PTC = papillary thyroid carcinoma; SAT = stool antigen test; UBT = urea breath test; NA = not applicable.

H. pylori before ^{131}I was 28.36%, whereas it was 18.18% after ^{131}I treatment. A significant decrease in ^{13}C-UBT was observed after ^{131}I treatment compared with before treatment ($P < 0.01$) (*14*).

Our results were significantly different from those of these 2 studies (*11*,*14*). In the present study, 51.8% (14 of 27) of patients were *H. pylori*–positive. We found that ^{131}I therapy at different doses, administered to patients with DTC or hyperthyroidism, did not eradicate *H. pylori* in 92.8% of cases 8 wk after treatment. The conflicting results may be explained by the diversity of the population and the virulence of the gastric mucosal bacteria of treated patients—a factor that was not assessed in this study. A milder degree of *H. pylori* colonization in the gastric mucosa may result in enhanced sensitivity to ^{131}I, as the infection is less extensive and the gastritis is generally nonatrophic. Meanwhile, our geographic region has the highest rate of *H. pylori* infection in Iran, and the cytotoxin-associated gene E $(cagE)^+$ genotype of the *H. pylori* significantly increases the risk of gastric cancer in this high-risk population (*15*).

In addition, these differences may be due to the experimental techniques used in each study to detect *H. pylori* infection. Invasive and noninvasive tests are applied to diagnose *H. pylori* infection. In invasive methods, including cultures, histology, and urea tests, biopsy samples obtained by upper gastrointestinal endoscopy are used. Noninvasive techniques include stool antigen tests, UBT, and serology. UBT is faster and cheaper than the others. Proton pump inhibitors, bismuth, and antimicrobial agents may interfere with this test by inhibiting urea activity. Moreover, other urea-producing microorganisms in the gastric mucosa can create false-positive results (*16*). Stool antigen testing is an inexpensive way to detect active *H. pylori* infection. Enzyme immunoassays and immunochromatography are 2 types of this test. Eradication of *H. pylori* infection is assessed by stool antigen testing. Hence, this test is useful before and after *H. pylori* therapy (*13*). In the present study, *H. pylori* infection was detected by stool samples, whereas Gholamrezanezhad et al. and Xu et al. (*11*,*14*) used UBT. In accordance with these findings, a study by Shmuely et al. (*17*) found that ^{131}I treatment did not eliminate *H. pylori* infection in Israeli patients. All 18 patients with DTC and *H. pylori* antigen–positive stool remained positive 3 mo after ^{131}I therapy, representing an eradication rate of 0% with an upper 95% confidence limit of 18.53% (*17*). Table 2 compares the findings of the present study with previous studies on eradication of *H. pylori* using ^{131}I.

CONCLUSION

In the current study, the effect of different doses of ^{131}I radiation on *H. pylori* in our local population of DTC or hyperthyroidism patients was investigated. Contrary to previous reports, ^{131}I failed to eradicate *H. pylori* infection, possibly because of the severe degree of *H. pylori* colonization in the gastric mucosa. Therefore, further investigation in different populations is needed.

DISCLOSURE

The study was supported and funded by the Deputy of Research and Technology, Ardabil University of Medical Sciences (IR.ARUMS.REC.1399.070). No other potential conflict of interest relevant to this article was reported.

KEY POINTS

QUESTION: Does ^{131}I prescribed in different doses (0.15–5.5 GBq) for DTC or hyperthyroid patients eliminate *H. pylori* infection?

PERTINENT FINDINGS: Different doses of ^{131}I radiation had no effect on *H. pylori* in our local population of patients with DTC or hyperthyroidism.

IMPLICATIONS FOR PATIENT CARE: ^{131}I radiation cannot be a rational treatment for the eradication of *H. pylori* in the people of our geographic region (Ardabil, Iran).

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