14C-urea breath test in patients undergoing anti-tuberculosis therapy

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Abstract

AIM: Urea breath test (UBT) is a non-invasive diagnostic test for detecting the presence of Helicobacter pylori (H pylori). In this study we evaluated the effect of anti-tuberculosis therapy on the results of 14C-UBT.

METHODS: Patients, with the diagnosis of tuberculosis (TB) who had a positive UBT at the point of starting anti-TB therapy, were included. None had a history of peptic ulcer disease or had taken antibiotics, bismuth compounds and/or PPI in the previous month. 14C-UBT was repeated at the end of the second month and one month after completion of treatment course.

RESULTS: Thirty-five patients (23 males) were enrolled. 14C-UBT was negative in all 35 patients (100%) at the end of the second month and remained negative in 30 cases (85.7%) at the end of the treatment course. One month after completion of treatment course, UBT remained negative in 13 patients (37.1%).

CONCLUSION: Our report underscores the need for caution while interpreting urea breath test results in patients undergoing anti-tuberculosis therapy. World J Gastroenterol 2005; 11 (11): 1712-1714

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INTRODUCTION

Helicobacter pylori (H pylori) is the most renowned factor among peptic ulcer risk factors[1][2]. Eradication of this germ has contributed to a significant reduction in the peptic ulcer prevalence[3][4]. Several drug regimens have been introduced for H pylori eradication[5][6]. Urea Breath Test (UBT) is currently the standard means of determining H pylori eradication. Some drugs, including antibiotics are known to lower the accuracy of this test. In the present study, we evaluated specifically the effect of a four-agent anti-tuberculosis therapy on the results of 14C-UBT in a group of patients with tuberculous and positive baseline UBT.

MATERIALS AND METHODS

All patients referred to Amir-Alam General Hospital from January 2002 to December 2003 with a diagnosis of tuberculosis (TB) were evaluated. TB had been documented based on clinical and laboratory findings and anti-tuberculosis treatment was ordered for all of them. Patients with a history of documented peptic ulcer before treatment or using Bismuth, proton pump inhibitors (PPIs), H2 blocker agents or antibiotics in the month before were excluded from the study. None of the enrolled patients had ever been treated for H pylori eradication or undergone gastric resection. UBT test was done for all patients at the time of starting anti-TB therapy and patients with positive tests were enrolled. The anti-TB regimen in all patients consisted of Isoniazid, Rifampicin, Ethambutol and Pyrazinamide for two months, after which the latter two drugs were stopped and the treatment was carried on with Isoniazid/Rifampicin until the end of the treatment course. Cases of spinal tuberculosis were planned for a 12-mo course of therapy, whereas a 6-mo course was considered for other types of tuberculous organ involvement.

14C-UBT was repeated three times for every enrolled patient: (1) at 2 mo (time of stopping Ethambutol/Pyrazinamide); (2) end of treatment course (mo 12 for spinal TB cases); (3) one month after completion of the anti-TB treatment course. The tests were all performed in the Nuclear Medicine Laboratory, Shariati Hospital, Tehran University of Medical Sciences, by a single team of specialized staff. Each overnight fasting patient was given 1 μCi (37 kBq) of 14C-urea.
H pylori colonizes gastric mucosa and elicits both inflammatory and immune lifelong responses, with release of various bacterial and host-dependent cytotoxic substances[8]. H pylori eradication can be established reliably by histology, rapid urease testing and the urea breath test (UBT). The UBT uses labeled urea (14C or 15N) that, in the presence of H pylori, is metabolized by urease to yield CO2. The labeled gas is absorbed across the gastric mucosa and subsequently measured in the patient’s expired breath.

Analysis of the results reported in studies in which urea breath-tests were evaluated against an accepted gold standard, confirms the great accuracy (sensitivity 97%; specificity 95%) of this technique[9].

There is general consensus[10-13] regarding the adverse effect of proton pump inhibitors (PPIs) on the UBT (false negative results range from 17% to 61%). Moreover, antibiotics and bismuth compounds reduce H pylori load such that infection may be undetectable. Thus, urea breath-tests should not be performed within 4 wk of receiving such drugs, whether given specifically to treat the infection or not[14].

In 1992, Mitchell found that a history of pulmonary TB might be associated with an increased prevalence of H pylori infection[15]. More recently, Woeltje assessed the prevalence of tuberculin skin test (TST) positivity in a cohort of 346 newly hospitalized patients. A history of peptic ulcer disease was one of the identified risk factors for a positive TST test (odds ratio: 4.53, P = 0.017)[16]. Increased risk of TB for persons with a history of peptic ulcer disease has also been reported[17]. H pylori is seen in high prevalence in some populations around the world[18] especially in regions having lower socioeconomic status[19,20]. The same is true for the distribution of tuberculosis which is, to a great extent, clustered in some developing countries[21]. Rationally, there seems to exist a population of considerable size, potentially exposed to both microorganisms.

**DISCUSSION**

*H pylori* is a slow-growing, microaerophilic, gram-negative bacterium, whose most striking biochemical characteristic is the abundant production of urease. This bacterium colonizes gastric mucosa and elicits both inflammatory and

### RESULTS

During the study period, 44 patients with a definite diagnosis of tuberculous infection were planned for anti-TB therapy. Three patients revealed a history of antibiotic therapy during the month before and were therefore excluded. Six more patients had negative or intermediate UBT results and were also excluded. Thirty-five patients including 23 males (age 17-55 years; mean age: 38.5) and 12 females (age 16-39 years; mean age: 24) were eligible for the study. Among the enrolled patients there were 12 pulmonary and 23 extra-pulmonary cases of TB including 5 patients with a diagnosis of vertebral tuberculous osteomyelitis (Table 1). None were critically ill or under treatment with immunosuppressive drugs.

At the end of the second month of therapy, UBT became negative in all 35 patients (100%). The test results at the end of the treatment course were still negative in 30 cases (85.7%). One month after completion of anti-tuberculosis therapy, UBT turned positive in 17 of 30 patients, so 22 (85.7%). One month after completion of anti-tuberculosis therapy, UBT turned positive in 17 of 30 patients, so 22 (85.7%). One month after completion of anti-tuberculosis therapy, UBT turned positive in 17 of 30 patients, so 22 (85.7%).

| Type of infection | Male | Female |
|-------------------|------|--------|
| Pulmonary TB      | 12   | 16-39  |
| TB adenitis       | 9    | 25     |
| TB enteritis      | 5    | 35     |
| TB osteomyelitis (vertebra) | 5 | 75 |
| Meningeal TB      | 2    | 35     |
| Peritoneal TB     | 2    | 35     |
| Total             | 35   | 35     |

### DISCUSSION

**Table 1** Patient characteristics

| Gender | Male | Female |
|--------|------|--------|
| Total  | 35   | 35     |

### DISCUSSION

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| Gender | Male | Female |
|--------|------|--------|
| Total  | 35   | 35     |

### DISCUSSION

**Table 2** 14C-urea breath test results among 35 patients during the course of anti-tuberculosis therapy

|                      | Baseline | End of 2nd mo of therapy | End of treatment course | One month after completion on therapy |
|----------------------|----------|--------------------------|-------------------------|--------------------------------------|
| Positive (%)         | 35 (100) | 0 (0)                    | 4 (11.4)                | 22 (62.9)                            |
| Negative (%)         | 0 (0)    | 35 (100)                 | 30 (85.7)               | 13 (37.1)                            |
Furthermore, the combination of drugs used in this study resulted in *H pylori* eradication in a minority of patients.

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