Do urea breath test (UBT) referrals for *Helicobacter pylori* testing match the clinical guidelines in primary care practice? A prospective observational study

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Abstract

**Background** Various international guidelines recommend the use of non-endoscopic tests [such as urea breath test (UBT)] for the evaluation of dyspeptic patients, unless endoscopy is clinically indicated.

**Aim** To assess adherence with guidelines for UBT referrals among primary care doctors in Israel.

**Methods** Patients referred by primary care doctors to an open-access UBT service were included in the study. Prior to the test, all patients were administered with a short questionnaire regarding their symptoms, previous and concomitant medications including previous *Helicobacter pylori* eradication.

**Results** The study sample consisted of 209 patients, aged 18–94 years, M/F = 74/135. The UBT was judged to be appropriate in 94 (45%) subjects, inappropriate in 93 (44.5%) subjects and appropriate but avoidable in 22 (10.5%) subjects, most of them asymptomatic patients following anti-*H. pylori* treatment. The inappropriate indications include 38 (18%) patients with suspected gastro-oesophageal reflux disease symptoms and 21 (10%) dyspeptic patients aged 45 years or more.

**Conclusion** Nearly 45% percent of UBT referrals in primary care practice were inappropriate, and a significant number of dyspeptic patients should have been referred to endoscopy. These findings show a substantial non-compliance with guidelines for *H. pylori* testing among primary care doctors.

Introduction

Dyspepsia is a common problem in primary care, where between 30% and 40% of the general population reports symptoms [1–3], and its management places a major clinical and economic burden on the health services.

*Helicobacter pylori* is the major cause of peptic ulcer disease (PUD), and it is also implicated in the pathogenesis of gastric cancer [4]. The diagnostic methods of *H. pylori* infection include non-invasive methods such as serology, urea breath test (UBT) and *H. pylori* stool antigen test, and invasive biopsy-based tests such as histology, bacterial culture and rapid urease test [5]. According to the Maastricht 3 Consensus Report, a ‘test and treat’ strategy for *H. pylori* infection is recommended in young (<45 years) dyspeptic patients according to the following criteria: (1) the presence of typical PUD symptoms, having excluded those with predominantly gastro-oesophageal reflux disease symptoms (GERD) or non-steroidal anti-inflammatory drug users; (2) confirmation of eradication of the organism after therapy in complicated PUD; (3) typical symptoms recurrence after eradication therapy for *H. pylori*; and (4) family history of gastric cancer [6]. The presence of alarm symptoms, a second treatment failure or age exceeding 45 years are considered an indication for referral to a gastroenterologist.

Despite its valuable diagnostic potential, our clinical impression is that UBT is overloaded with inappropriately referred patients. This may lead to inappropriate and unnecessary treatments.

The aim of this study was to evaluate the indications for UBT used by primary care doctors and to examine the appropriateness of these indications to the accepted guidelines of the Maastricht Consensus Report.
Material and methods

Subjects

A total of 209 consecutive patients (74 men, 135 women) referred to six different stations of the *H. pylori* central laboratory for 13C-Urea breath test were included. Prior to testing for *H. pylori*, the patients were administered with a short questionnaire regarding their symptoms and concomitant medications including previous *H. pylori* eradication. The indication for referral to UBT – according to the referring doctor – was taken from the computerized medical records of each patient.

Questionnaire

Participants were questioned regarding their upper abdominal symptoms, history of prior UBT and/or eradication treatment for *H. pylori* and the use of H2 antagonists or proton pump inhibitors (PPIs) during the week prior to the test. They were also asked whether they were instructed not to use these medications by the referring doctor prior to the test.

Each patient underwent the urea breath test by carbon 13 using a mass spectrometer [Analytical Precision 2003™ device (Norwich, Cheshire, UK)]. 75 mg of urea labeled with 13C, in 150 mL of orange and lemon juice, was administered. Breath samples were collected twice, at 0 and 30 minutes. The ratio of 12C to 13C was measured at both time points. Results greater than 4 (cut-off value) were considered positive.

Referrals to UBT were defined appropriate according to the Maastricht guidelines.

The study protocol was conducted in accordance with the declaration of Helsinki, and ethics committee approval was obtained before the study commenced. All the subjects who agreed to participate in the study signed informed consents.

Statistical analysis

Statistic tests were done using SPSS software, version 14.0 (SPSS Inc., Chicago, IL). Between-group differences were evaluated by using the Pearson chi-square for categorical variables. All *P*-values were two-sided and considered significant at 0.05.

Results

The study sample consisted of 209 patients, aged 18–94 years, 74 (35%) men and 135 (65%) women (Table 1). The gender and age distributions were similar in the *H. pylori* positive and negative patients.

According to the medical records of the participants, the most prevalent indication for the test was abdominal pain, in 90 patients (43%), of which 40% were tested positive for *H. pylori*. Other indications are specified in Fig. 1 and Table 2.

The UBT referrals were judged to be appropriate in 94 subjects (45%). Most of them were patients aged <45 years presented with primary upper abdominal pain – 69 patients (33%). The second most common indication was ongoing dyspeptic symptoms following one course of anti-*H. pylori* treatment in patients aged <45 years – 19 patients (9%). The UBT referrals were judged to be inappropriate in 95 subjects (45%), 38 of them (18.2%) with heartburn or other symptoms indicating GERD – in any age – and 46 patients (22%) aged >45 years presenting with new or continuous dyspeptic symptoms. The last category of UBT referrals was the appropriate but avoidable, which was found in 22 subjects (10.5%) (Table 2).

*H. pylori* positive was found in 36 out of 90 patients (40%) with primary upper abdominal pain, and in 14 out of 36 patients (38.9%) with heartburn without significant difference (*P* = 0.93).

Only 16 patients (8%) used PPIs the week prior to the UBT (five of whom were tested positive anyway). A total of 159 patients reported avoiding PPI ‘according to the doctor’s orders’ and the rest did not need medication prior to the test.

Discussion

Clinical practice guidelines for dyspepsia have been published for more than 10 years and have been widely disseminated to primary
Care doctors all over the world – including Israel – through professional publications, meetings and local workshops [6–9]. The present study shows that nearly 55% of UBT referrals were inappropriate or appropriate but avoidable. Similar findings have been found by Perri et al. in Italy [10]. In their study, UBT was found to be appropriate in 63.3% of patients, inappropriate in 14.5% and appropriate but avoidable in 22.1% of patients.

What may be the reasons for the high inappropriate referral rate for UBT in our study? Most of the inappropriate referrals concerned the application of the ’test and treat’ strategy in patients who are at risk of severe organic disease and should have been referred for endoscopy. This includes 57 patients aged 45 years or older presenting with new-onset dyspepsia that constituted 60% of the 95 inappropriate referrals in our study.

Results from several recent surveys have suggested that significant confusion exists with respect to the understanding of the relationship between H. pylori infection and the pathogenesis, diagnosis and treatment of upper gastrointestinal (GI) diseases [11–14]. The major uncertainty surrounds the management of patients with dyspepsia where the general practitioner needs to make a decision whether to prescribe an empirical anti-acid treatment to test for H. pylori infection and treat if positive, or to refer patients to a specialist for endoscopy. It seems that in many cases, referral for UBT serves as a compromise between the first alternative, of prescribing empirical anti-acid treatment without an attempt to establish a definitive diagnosis, and the invasive alternative of referring the patient to endoscopy, which might be considered too aggressive. For example, in patients older than 45 years with mild symptoms, a non-invasive strategy might be considered more attractive as well as more accessible. The disadvantage of this strategy is the possibility of missing upper GI malignancies, depending on its local prevalence.

The second group of inappropriate referrals was those with presumed GERD that constituted 27/95 (28.4%) of the referrals. Eleven more patients (11.6%) were both above the age of 45 years and suspected to have GERD. Previous studies did not find a causal link between H. pylori and GERD [15], and most of clinical guidelines including that of Maastricht 3 do not recommend H. pylori testing for patients who have only GERD symptoms [6–9]. Although there is a justification to refer some patients with GERD-like symptoms for H. pylori testing to exclude or eradicate infection before long-term treatment with PPI in order to prevent accelerated gastric atrophy [16]; this was not the reason for the referrals in the current study.

In the present study, we defined post-treatment testing in asymptomatic patients as inappropriate. Guidelines are mixed as to recommendations for routine post-treatment testing to document successful H. pylori eradication. Since the overall eradication rate of H. pylori is around 75%, some guidelines recommend routine post-treatment testing [6], where others – and this was also our policy – recommend post-treatment testing only for patients with ongoing symptoms or those with complicated peptic ulcer disease, such as bleeding [9,17].

Over the past 17 years, the status of H. pylori infection and its relation to upper gastrointestinal diseases has evolved from a medical curiosity to a well-recognized and extensively investigated pathogen of considerable clinical significance. Because of its extreme high prevalence in the general population and the existence of several controversies, a proper approach to the management of H. pylori infection is of crucial importance. This has led to the development and publication of international and national guidelines that present a unique challenge. The current study, as well as other studies from all over the world, demonstrate only partial adherence of medical communities to these guidelines recommendations [18,19].

How can we improve the implementation of these guidelines, especially in primary care practice?

Adherence to clinical guidelines depends on several factors. These include postgraduates’ implementation programs as well as monitoring and feedback on performance.

An important factor for optimal implementation of guidelines is cooperation between primary and secondary care specialists. The majority of guidelines for the management of H. pylori infection has been produced by specialists and has been criticized for their failure to address the issues that are important in primary care [20]. It has been shown that clinicians are more likely to follow guidelines if they have played some part in formulating them, and internally developed guidelines are often more successful than externally developed national guidelines [21].

In conclusion, the present study demonstrates that the diagnosis and treatment of H. pylori infection are still suboptimal and somewhat removed from what is recommended by current practice guidelines. It seems, therefore, that the publication of recommendations should be accompanied by enabling strategies to motivate and facilitate their implementation. Such steps would
greatly improve patient care and make better use of limited resources.

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