

ORIGINAL PAPERS

Almagate interference in breath test results for the diagnosis of *Helicobacter pylori* infection

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ABSTRACT

Background: Infection by *Helicobacter pylori* is common and affects both genders at any age. The ¹³C-urea breath test is a widely used test for the diagnosis of this infection. However, multiple drugs used for the treatment of *Helicobacter pylori* infection symptoms have interactions with this breath test that generate false negative results. This observational study was to assess the potential interaction between almagate and the breath test.

Methods: Thirty subjects on almagate therapy who underwent a breath test were included. If the result was negative, almagate was withdrawn for a month and the breath test was then repeated.

Results: In general, 51.9 % of assessed subjects had a negative result after the first test, and 100 % of these also had a negative result after the second test.

Conclusions: It was concluded that the use of almagate does not interfere in breath test results. These results provide a drug therapy option for the treatment of symptoms associated with *Helicobacter pylori* infection during the diagnostic process.

Key words: Breath test. Omeprazole. Almagate. *Helicobacter pylori*.

Pons C, Maisterra S, Salord S, Pla A, Asensio D, Fernández FJ, Traveria G, Roura G. Almagate interference in breath test results for the diagnosis of *Helicobacter pylori* infection. *Rev Esp Enferm Dig* 2014;106:448-451.

Acknowledgments: The present study was made possible thanks to the support of Almirall, S.A. Barcelona, Spain.

Received: 31-03-2014

Accepted: 27-08-2014

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INTRODUCTION

Helicobacter pylori infection is one of the commonest chronic infectious diseases worldwide (1), and is directly related to chronic gastritis, adenocarcinoma, and predisposition to gastroduodenal ulcer disease (2). Prevalence may vary from 20 % to 60 % according to geographic region (3). In a healthy population from Madrid, the prevalence of *Helicobacter pylori* infection was found to be 60.3 % (4), a higher percentage as compared to figures detected in Germany (5) or the United States (6).

The ¹³C-urea breath test (UBT) is a common non-invasive test that provides an accurate diagnosis of *Helicobacter pylori* infection. However, previous studies showed that the use of proton pump inhibitors, a class of drugs widely used to relieve symptoms from this infection, may change UBT results (7-9). Graham et al. observed that the use of omeprazole is associated with a decrease in urease activity for patients infected with *Helicobacter pylori* (p = 0.031). Thirty-three percent of infected patients obtained a false negative UBT result. After 14 days following omeprazole therapy withdrawal all these patients had a positive result and baseline urease activity was back in place (9). The use of omeprazole has also been shown to interfere in *Helicobacter pylori* serology test results. In a study performed in Italy, omeprazole administration for two weeks in patients defined as positive reduced the sensitivity of antigen serology tests by 22 %. After drug discontinuation for two weeks, all patients obtained a positive result with this same test (7).

An alternative to proton pump inhibitors is almagate, but whether this drug interferes in UBT sensitivity had not been analyzed to this day. The goal of our study was to assess the potential interference of almagate in UBT results for the diagnosis of *Helicobacter pylori* infection, and to describe patient profiles according to UBT results.

METHODS

This was an observational, single-center, pilot study carried out following the standard clinical practice of Primary Care Center Just Oliveres (Hospitalet de Llobregat, Barcelona, Spain). Participants included subjects ≥ 18 years of age scheduled to undergo UBT while on almagate, who had received no proton pump inhibitors or antibiotics in the last 30 days. Doses administered were 1.5 grams every 12 hours for 30 days until the day before the breath test, which was performed after fasting for 8 to 10 hours. Recruitment took place from November 2011 to May 2012. All participants underwent UBT for the diagnosis of *Helicobacter pylori* infection. Only subjects with a negative result had a repeat test after one month off almagate. UBT was performed using the TAUKIT kit with 100 mg of ^{13}C -urea (Isomed Pharma).

All participants gave their written informed consent. The study was conducted according to Declaration of Helsinki principles and good clinical practice tenets (ICH guideline for Good Clinical Practice, 1996). The study was submitted for consideration to the Ethics Committee/Review Board of IDIAP Jordi Gol i Gurina.

Given the absence of medical literature on the interference of almagate in UBT results, sample size could not be established with statistical accuracy. A pilot study was decided upon, which would include 30 participants. Qualitative variables were described using absolute and relative frequencies. Mean and standard deviation (SD) were chosen to describe quantitative variables. The chi-squared test and Fisher's test were used to compare qualitative variables, according to variable type. For comparison of quantitative variables the Mann-Whitney nonparametric U-test was used. Statistical analyses were performed with the SAS 9.3 software package.

RESULTS

Of all subjects recruited by the study, three were excluded because of unavailable UBT results, hence the analysis was carried out in 27 participants (90 % of the eligible population). In all, 70.4 % ($n = 19$) were females, mean age was 56.9 years ($\text{SD} = 17.4$), mean BMI was 26.2 kg/m^2 ($\text{SD} = 4.9$), and 96.2 % were Hispanics. Mean time from treatment onset to first test was 30.2 days ($\text{SD} = 1.4$). Table I includes all histories of gastric disease and gastric symptoms. Among participants, 74.1 % reported a history of gastric or duodenal ulcer, and 92.6 % suffered from dyspepsia; 44.4 % had been previously diagnosed with *Helicobacter pylori* infection.

As regards the first UBT performed, 51.9 % of participants had a negative result. Mean time between the first and second tests was 153.4 days ($\text{SD} = 76.3$). A first negative test followed by a second positive one was considered a false negative result. No false negative results were obtained.

Table II lists subject characteristics according to UBT result –38.5 % of participants with a positive result and 21.4 % of those with a negative result were males. Differences were not statistically significant (Fisher's test, $p > 0.05$). The history of gastric disease was similar for both UBT result groups. Symptoms according to the presence or absence of infection by *Helicobacter pylori* are also listed in table II. The percentage of participants with abdominal pain and heartburn was higher among individuals with *Helicobacter pylori* infection as compared with non-infected subjects. Of all participants with a positive result, 69.2 % had abdominal pain and 61.5 % had heartburn, as compared with 14.3 % and 14.3 % of those with a negative result, respectively. These were the only statistically significant differences observed according to UBT results. All subjects had dyspepsia, and anthropometric measurements were similar in both groups.

DISCUSSION

Proton pump inhibitors such as omeprazole are among the most widely used drugs against infection with *Helicobacter pylori*. However, this drug has often been seen to interfere with UBT providing false negative results (7). Omeprazole may reduce *Helicobacter pylori* bacteria load and inhibit gastric urease activity. It is not until two weeks after omeprazole therapy discontinuation that UBT results become really reliable (9). This is why, in clinical practice, health care providers must forbid patients from using this drug before a diagnosis of infection with *Helicobacter pylori* is reached. Our results open up a new alternative to omeprazole in order to alleviate infection manifestations without interfering with its diagnosis.

Table I. Gastric disease history and manifestations

	<i>n</i>	%
<i>Gastric disease history</i>		
No	7	25.9
Yes	20	74.1
Duodenal ulcer	6	22.2
Gastric ulcer	3	11.1
MALT lymphoma	3	11.1
Reflux disease	2	7.4
Other	6	22.2
<i>Gastric symptoms</i>		
Dyspepsia	25	92.6
Abdominal pain	11	40.7
Heartburn	10	37.0
Mild nausea	4	14.8
Other	2	7.4

MALT: Mucosa-associated lymphoid tissue. Percentages estimated for total evaluable participants ($n = 27$). A participant may present with more than one history or symptom at a time.

Table II. Characteristics and gastric manifestations of patients per UBT result

	Positive		Negative		p
	n	Mean (SD) or %	n	Mean (SD) or %	
<i>Characteristics</i>					
Age (yrs)	13	54.5 (18.7)	14	59.3 (16.4)	0.595
Weight (kg)	13	65.6 (14.1)	14	70.1 (13.0)	0.317
Height (cm)	13	162.5 (12.2)	14	159.7 (6.1)	0.866
BMI (kg/m ²)	13	24.8 (4.5)	14	27.5 (5.1)	0.227
<i>Symptoms</i>					
Dyspepsia	11	84.6	14	100	0.222
Abdominal pain	9	69.2	2	14.3	0.004
Heartburn	8	61.5	2	14.3	0.018
Mild nausea	2	15.4	2	14.3	1.000
Other	0	0	2	14.3	0.481

UBT: ¹³C-Urea breath test; SD: Standard deviation; BMI: Body mass index. Percentages were estimated for total participants in each group. A subject may present with more than one symptom at a time. The Mann-Whitney U-test, Chi-squared test and Fisher test were used to analyze differences between groups according to variable characteristics.

The present pilot study is the first one to show that alginate therapy does not interfere in UBT results for the diagnosis of infection with *Helicobacter pylori*. Of all subjects evaluated, 51.9 % had a negative result in the first test. When the same test was repeated to all these participants following alginate discontinuation 100 % of cases were still negative, and no false negatives were observed. It was concluded that alginate use does not interfere in UBT results for the diagnosis of infection with *Helicobacter pylori*.

The fact that this was a pilot study with a limited sample size should be highlighted. However, these results show that there is a need for a multicenter study allowing greater statistical power.

REFERENCES

1. Cave DR. Transmission and epidemiology of *Helicobacter pylori*. *Am J Med* 1996;100:12-8.
2. Brown LM. *Helicobacter pylori*: Epidemiology and routes of transmission. *Epidemiol Rev* 2000;22:283-97.
3. Calvet X, Ramírez Lázaro MJ, Lehours P, Mégraud F. Diagnosis and epidemiology of *Helicobacter pylori* infection. *Helicobacter* 2013;18:5-11.
4. Sánchez Ceballos F, Taxonera Samsó C, García Alonso C, Alba López C, Sainz de los Terreros Soler L, Díaz-Rubio M. Prevalence of *Helicobacter pylori* infection in the healthy population of Madrid (Spain). *Rev Esp Enferm Dig* 2007;99:497-501.
5. Breuer T, Sudhop T, Hoch J, Sauerbruch T, Malfertheiner P. Prevalence of and risk factors for *Helicobacter pylori* infection in the western part of Germany. *Eur J Gastroenterol Hepatol* 1996;8:47-52.
6. Everhart JE, Kruszon-Moran D, Perez-Perez GI, Sue Tralka T, McQuillan G. Seroprevalence and Ethnic Differences in *Helicobacter pylori* Infection among Adults in the United States. *J Infect Dis* 2000;181:1359-63.
7. Manes G, Balzano A, Iaquinto G, Ricci C, Piccirillo MM, Giardullo N, et al. Accuracy of the stool antigen test in the diagnosis of *Helicobacter pylori* infection before treatment and in patients on omeprazole therapy. *Aliment Pharmacol Ther* 2001;15:73-9.
8. Parente F, Sainaghi M, Sangaletti O, Imbesi V, Maconi G, Anderloni A, et al. Different effects of short-term omeprazole, lansoprazole or pantoprazole on the accuracy of the (13)C-urea breath test. *Aliment Pharmacol Ther* 2002;16:553-7.
9. Graham DY, Opekun AR, Hammoud F, Yamaoka Y, Reddy R, Osato MS, et al. Studies regarding the mechanism of false negative urea breath tests with proton pump inhibitors. *Am J Gastroenterol* 2003;98:1005-9.