Eradication Therapy in *Helicobacter pylori*-Positive Patients with Halitosis: Long-Term Outcome

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Key Words

Halitosis · Eradication therapy · *Helicobacter pylori* ·
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Abstract

Objective: The aim of this study was to investigate the incidence and long-term outcome of halitosis before and after eradication therapy in patients with functional dyspepsia and *Helicobacter pylori* infection. **Subjects and Methods:** Halitosis and dyspepsia-related symptoms were investigated by way of a questionnaire. Only patients with functional dyspepsia, *H. pylori* infection and no histological evidence of atrophy were included in the study. A total of 18 patients fulfilled these criteria and completed the study. Four to six weeks after the end of eradication treatment, endoscopy or [¹³C] breath test was performed to check for *H. pylori* in the gastric mucosa. Halitosis and dyspeptic symptoms were re-evaluated during and at the end of follow-up. **Results:** *H. pylori* infection was eradicated in all patients, in the 14/18 patients (77.8%) with triple drug therapy, and the 4/18 patients (22.2%) with quadruple drug therapy. During the follow-up period (mean 55.8 ± 21.3 months (range 6–108 months)) resolution of halitosis was observed in 16/18 patients (88.9%), while 2 patients (11.1%) ($p < 0.001$) continued to present with halitosis. Also, eradication therapy resulted in statistically significant relief of all dyspeptic symptoms,

except bloating. **Conclusion:** Eradication of *H. pylori* in patients with functional dyspepsia and halitosis results in sustained resolution of halitosis during long-term follow-up in the majority of cases. This finding supports the existence of a link between *H. pylori* infection and halitosis and suggests that *H. pylori* eradication might be considered in patients with halitosis.

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Introduction

Halitosis (oral malodour or ‘bad breath’) is a general term used to describe an unpleasant or offensive odour emanating from the oral cavity. Halitosis is a symptom that causes social discomfort because no one enjoys conversing with a person who emits a fetid odour from the mouth [1]. Due to the importance of social interactions in contemporary society, many are becoming more concerned and paying more attention to this problem. The prevalence of halitosis has been reported to range between 6 and 24%, although precise epidemiological data are missing [2, 3]. Despite the reported high prevalence of breath malodour, only a few patients seek treatment, perhaps because most people suffering from bad breath remain completely unaware they in fact have the condition. Halitosis is classified into genuine halitosis, pseudo-

halitosis and halitophobia [4]. Genuine halitosis includes physiologic and pathologic halitosis [4]. Physiologic halitosis, also termed transient halitosis, has its origin in the dorsum of the tongue, is self-limited, and does not prevent the patient from carrying out a normal life [4]. On the contrary, pathologic halitosis is permanent and prevents the patient from carrying out a 'normal' life [4]. Depending on its origin, pathologic halitosis is categorized into oral and extraoral halitosis [4]. In 80–90% of cases, halitosis originates in the mouth due to inadequate plaque control, periodontal disease, dry mouth, faulty restorations, and excessive bacterial growth on the posterior third of the dorsal surface of the tongue [5]. Oral halitosis is the result of microbial putrefaction, during which volatile sulphur compounds (VSC) and other volatile compounds are produced [6]. In the remaining 10–20% of cases, bad breath is caused by systemic disorders such as hepatic, pancreatic and renal insufficiency, trimethylaminuria, respiratory tract infection, medication, smoking or ingestion of garlic, onion, alcohol or paraldehyde, whose volatile products are excreted by the lungs or in saliva [1, 6, 7]. In pseudo-halitosis, oral malodour does not exist but the patient believes that he or she has oral malodour [4]. In halitophobia, after treatment for either genuine halitosis or pseudo-halitosis, the patient still believes that he or she has halitosis [4].

The three main methods of diagnosing halitosis are gas chromatography, organoleptic measurement, and sulphide monitoring [8]. Gas chromatography is considered the gold standard for measuring oral malodour because it is specific for VSC, the main cause of oral malodour [8]. Organoleptic measurement is a sensory test scored on the basis of the examiner's perception of a subject's oral malodour [8]. Sulphide monitors analyze for total sulphur content of the subject's mouth air, but are not specific for VSC [8].

Treatment of pathologic halitosis depends on the source of the malodour. Oral halitosis can be successfully treated by a regimen that includes tooth and tongue brushing on a routine basis and possibly the usage of mouth rinses as a temporary measure [8]. The management of oral halitosis also involves maintenance of plaque control, elimination of active periodontal disease, and correction of faulty restorations [8]. Extraoral halitosis should be managed by identifying and targeting the underlying systemic condition, if this is possible [8]. Physiologic halitosis usually does not need any therapy [8]. Patients with pseudo-halitosis need to be counselled that the intensity of their malodour is not beyond a socially acceptable level [8]. Finally, patients with halitophobia

should receive treatment by a psychiatrist or psychological specialist [8].

There are a few reports [9–12] linking halitosis with *Helicobacter pylori* and showing the effect of eradication therapy on the treatment of halitosis. However, there are no data on the long-term effect of eradication of *H. pylori* on halitosis. We report the long-term effects of *H. pylori* eradication in a cohort of 18 Greek patients with objective halitosis and *H. pylori* infection.

Patients and Methods

The study included 18 patients with functional dyspepsia, 10 males and 8 females, with a mean age of 40.7 ± 10.9 years (range 18–68 years) (table 1). All patients suffered from objective halitosis, which was confirmed by questions to the patients and their relatives, since some patients were not aware of their problem and others mistakenly sensed a fetid breath odour. The patients were considered to have had halitosis when bad breath was reported during the 3 previous months. Symptoms of dyspepsia were investigated by means of a questionnaire that investigated epigastric pain, bloating, nausea and early satiety before and after eradication of *H. pylori*, and at the end of follow-up. In all patients, known local and systemic causes of halitosis were excluded on the basis of clinical history, biochemical serum investigations, odontologist's and otorhinolaryngologist's examinations, esophagogastroduodenoscopy and abdominal ultrasound scan. Individuals who were on antibiotics, proton pump inhibitors, H_2 receptor antagonists, NSAIDs or antihistaminic drugs were excluded.

In each case, four gastric biopsy specimens were collected from the antrum and corpus of the stomach. *H. pylori* status was determined histopathologically by examining slides prepared with hematoxylin and eosin, and Giemsa staining. A biopsy specimen was also taken from the antrum for CLO testing.

All subjects were prescribed a 10-day course of triple drug eradication therapy (20 mg omeprazole, 500 mg clarithromycin and 1,000 mg amoxicillin, all twice daily). In cases of eradication failure, a 10-day course of quadruple drug therapy (20 mg omeprazole twice daily, 600 mg bismuth subcitrate twice daily, 500 mg metronidazole twice daily, and 500 mg tetracycline, 4 times daily) was administered.

Four to six weeks after completion of eradication therapy, the symptom of halitosis was re-evaluated and repeat endoscopy or urea breath test was performed to assess *H. pylori* status in the gastric mucosa.

In the follow-up period (every 3 months for the first year and annually afterwards), apart from the patients' own perception of halitosis, the same relatives who were interviewed in the index visit were required to express their opinion by phone about the presence of halitosis.

Statistical Analysis

Symptom resolution statistics were addressed using the Wilcoxon signed rank test to compare paired data. A p value <0.05 was considered statistically significant. The statistical analysis was performed using the statistical program SPSS (Statistical Package for Social Sciences, Version 10.0, Chicago, Ill., USA).

Table 1. Patients' characteristics

Case	Sex	Age years	Before <i>H. pylori</i> eradication therapy (duration), months		Follow-up months
			halitosis	dyspeptic symptoms	
1	M	49	24	29	108
2	M	18	6	21	29
3	M	47	12	19	73
4	F	43	12	21	72
5	M	28	8	17	74
6	F	37	18	33	78
7	M	43	18	27	52
8	F	46	24	35	48
9	M	52	38	49	50
10	F	31	4	17	54
11	M	37	36	53	58
12	F	29	12	26	50
13	M	47	24	38	42
14	F	34	14	31	51
15	M	40	8	27	49
16	F	43	9	29	54
17	F	40	7	25	57
18	M	68	36	47	6
Mean $\pm$ SD (range)		40.7 $\pm$ 10.9 (18–68)	17.2 $\pm$ 10.9 (4–38)	30.2 $\pm$ 10.7 (17–53)	55.8 $\pm$ 21.3 (6–108)

Results

The mean duration of halitosis and dyspeptic symptoms prior to enrolment was 17.2 ± 10.9 (range 4–38) months, and 30.2 ± 10.7 (range 17–53) months, respectively (table 1). Endoscopy showed a normal profile in all patients. Histology showed antral gastritis in all patients, with mild inflammation in 11 patients (61.1%) and moderate inflammation in 7 patients (38.9%). No patient showed body mucosal inflammation (i.e. pangastritis).

Assessment of bacterial positivity was done on the first examination in all patients with endoscopy and biopsies for histology and CLO test. Eradication of *H. pylori* was tested with re-endoscopy and biopsies in 13 patients (72.2%) and with [^{13}C]urea breath test in 5 patients (27.8%). Triple drug therapy successfully eradicated *H. pylori* in 14/18 patients (77.8%). In the 4/18 patients (22.2%) who remained *H. pylori* positive after triple drug therapy, quadruple drug therapy successfully eradicated the bacterium.

During the follow-up period (mean 55.8 ± 21.3 (range 6–108) months), halitosis did not recur in 16/18 patients (88.9%), while 2 patients (11.1%) ($p < 0.001$) continued

Table 2. Halitosis and dyspeptic symptoms before and after *H. pylori* eradication therapy

Symptoms	Before treatment (n = 18)	After eradication therapy (n = 18)	p value
Halitosis	18 (100%)	2 (11.1%)	<0.001
Epigastric pain	10 (55.5%)	1 (5.5%)	<0.05
Bloating	11 (61.1%)	8 (44.4%)	NS
Early satiety	11 (61.1%)	6 (33.3%)	<0.05
Nausea	9 (50%)	1 (5.5%)	<0.05

NS = Not significant.

to complain of halitosis despite successful eradication of *H. pylori* (table 2). There were no differences between patients in whom halitosis resolved and those in whom halitosis persisted. In patients in whom halitosis resolved, this was noticed immediately at the first visit after successful eradication of *H. pylori*.

The dyspeptic symptoms that resolved with eradication therapy were epigastric pain (55.5 vs. 5.5%, $p < 0.05$), early satiety (61.1 vs. 33.3%, $p < 0.05$) and nausea (50 vs. 5.5%, $p < 0.05$) (table 2). Despite the decrease in the reporting of bloating after eradication therapy (61.1 vs. 44.4%), this difference was not significant (table 2).

Discussion

Halitosis generally arises as a result of the bacterial decomposition of food particles, cells, blood and some chemical components of saliva. Thus, 80–90% of cases of halitosis arise in the mouth [1]. Peaks of hydrogen sulphide, methyl mercaptan and dimethyl sulphide characterize saliva chromatograms from patients with halitosis [13, 14].

The possibility of gastrointestinal causes for halitosis is a more contentious issue; some researchers argue that because of the gastrointestinal system's functional isolation from the respiratory pathways, and since the normal state of the esophagus is one of collapse, breath odour should not necessarily indicate anything untoward about gastrointestinal function [15]. Halitosis has been reported in association with hepatitis, colonogastric fistula (a rare complication of Crohn's disease) [16], aorto-enteric fistula [17] and various diverticula [18, 19].

A possible link between the bacterium *H. pylori* and breath odour was first suggested by Marshall et al. [20]. In fact, in 1985 he ingested a culture of *H. pylori* to provoke gastritis in order to fulfil Koch's postulates. On this occasion, his colleagues noted that his breath was 'putrid'. In 1992, Tiomny et al. [9] reported an impressive improvement of subjective halitosis after *H. pylori* eradication in three couples, in which one or both members suffered from marked halitosis. An Italian study [11] on the relationship between *H. pylori* infection and halitosis found a highly significant correlation between the elimination of *H. pylori* infection and the disappearance of halitosis (measured by sulphide compound assay). The study also found that in the presence of *H. pylori*, chlorhexidine rinses might not be completely effective against halitosis. Recently, Serin et al. [12] investigated the frequency of halitosis and other symptoms of dyspepsia in *H. pylori*-positive dyspeptic patients before and after eradication therapy. They found that when other diseases or conditions associated with halitosis in patients with non-ulcer dyspepsia (NUD) are ruled out, *H. pylori* eradication is effective in eliminating breath malodour, and they suggested that under these circumstances and in

light of the success of treatment, halitosis may be considered an indication for *H. pylori* eradication.

Despite the small number of patients in our study, our findings strongly suggest that the symptom of halitosis is effectively resolved with long-term follow-up of *H. pylori*-positive patients who have had successful eradication therapy, despite the fact that breath sulphide compounds were not measured to document an objective correlation between these two factors. With a mean follow-up of 55.8 ± 21.3 (range 6–108) months and with 88.9% of patients being free of symptoms of halitosis, our study supports the theory that there is a link between *H. pylori* and halitosis.

Recent reports [21, 22] have confirmed the existence of *H. pylori* in the oral cavity, which indicates the presence of this organism in the mouth as a possible origin of halitosis. Unfortunately, we did not study the oral cavity of our patients for *H. pylori* infection and therefore cannot discriminate whether resolution of halitosis results from the eradication of *H. pylori* from the oral cavity, from the antrum, or both. Whether the effect of *H. pylori* on bad breath is limited to sulphides or associated with the production of other substances such as ammonia is yet undetermined [23]. In fact, the accumulation of ammonia in the blood of patients with renal or hepatic failure and its excretion through the lungs is known to induce halitosis [23, 24]. On the other hand, the contribution of ammonia produced by *H. pylori* to the systemic level depends on different factors (bacterial amount and distribution, host response) [23]. The most important factor is hepatic function, since *H. pylori* infection is able to induce hyperammonemia only in cirrhotic patients [23]. Nevertheless, hepatic and renal disease were criteria for exclusion in our study.

However, there are still unanswered questions about the link of halitosis with *H. pylori* infection: (a) Why is halitosis present in only a small percentage of *H. pylori*-positive patients while the bacterium is very common worldwide? (b) Through what mechanism does the bacterium contribute to halitosis? (c) Why do some patients (two in our study) continue to have halitosis despite successful eradication of *H. pylori*?

Currently, eradication treatment of *H. pylori* infection in patients with NUD has yielded conflicting results. Two major investigations done by Talley et al. [25, 26] showed that eradication of *H. pylori* infection is unlikely to relieve symptoms in patients with NUD, and the findings from a recent meta-analysis [27] also gave little support to the use of eradication therapy in these patients. On the other hand, in another study of NUD patients, McColl et al.

[28] showed that treatment with omeprazole and antibiotics was more effective than omeprazole alone in terms of achieving symptom resolution. Most of these studies used relief of upper abdominal pain or discomfort as the basis for calculating rates of treatment success. In our patients, eradication therapy of *H. pylori* infection resulted in statistically significant relief of all dyspeptic symptoms except bloating.

Conclusion

Eradication of *H. pylori* in patients with functional dyspepsia and halitosis results in sustained resolution of halitosis during long-term follow-up in the majority of cases. This finding supports the existence of a link between *H. pylori* infection and halitosis and suggests that *H. pylori* eradication might be considered in patients with halitosis.

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