CURRENT THERAPEUTIC RESEARCH
VOLUME 67, NUMBER 5, SEPTEMBER/OCTOBER 2006

Quality of Life in Patients with Functional Dyspepsia: Short- and Long-Term Effect of *Helicobacter pylori* Eradication with Pantoprazole, Amoxicillin, and Clarithromycin or Cisapride Therapy: A Prospective, Parallel-Group Study

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ABSTRACT

Background: Quality of life (QOL) is impaired in functional dyspepsia (FD). Little is known about the effects of different therapies on the QOL profile in patients with this condition.

Objectives: The aims of this study were to measure baseline QOL in patients with FD and to assess changes in QOL over time associated with *Helicobacter pylori* eradication and prokinetic treatment. The primary and secondary end points were the improvement in QOL 6 weeks and 1 year after successful eradication of the infection or prokinetic therapy.

Methods: This 1-year, single-center, prospective, open-label, controlled, parallel-group trial was conducted at the Department of Gastroenterology, Ferencváros Health Centre, Budapest, Hungary. The Functional Digestive Disorder Quality of Life (FDDQoL) Questionnaire (MAPI Research Institute, Lyon, France) was translated and validated previously in Hungarian. Male and female subjects aged 20 to 60 years were enrolled and classified as *H pylori* positive (HP+), *H pylori* negative (HP–) with FD, or healthy (control group). The HP+ patients received pantoprazole 40 mg BID + amoxicillin 1000 mg BID + clarithromycin 500 mg BID for 7 days, followed by on-demand ranitidine (150–300 mg/d) for 1 year. The HP– patients received the prokinetic cisapride 10 mg TID for 1 month, followed by on-demand cisapride (10–20 mg/d) for 1 year. The FDDQoL questionnaire was completed by all 3 groups on enrollment, at 6 weeks, and 1 year.

Results: A total of 101 HP+ patients, 98 HP– patients, and 123 healthy controls were included in the study (185 women, 137 men; mean age, 39.0 years). The mean (SD) baseline QOL scores were significantly lower in the HP+ group (53.3 [9.6]; 95% CI, 54.4–58.2) and the HP– groups (50.0 [9.8]; 95% CI, 58.0–62.0) compared with that in healthy controls (76.2 [8.7]; 95% CI, 74.6–77.8) (both, $P < 0.001$). Analysis of the short-term domain scores found that the HP+ group had significantly decreased scores in 6 of 8 domains: daily activities ($P = 0.005$),

Accepted for publication September 25, 2006.
doi:10.1016/j.curtheres.2006.11.001
0011-393X/06/$19.00

anxiety level ($P = 0.02$), diet ($P = 0.008$), sleep ($P < 0.001$), discomfort ($P = 0.004$), and disease control ($P = 0.02$); the HP– group had significantly decreased scores in 5 of 8 domains: daily activities ($P < 0.001$), diet ($P = 0.004$), sleep ($P = 0.005$), discomfort ($P < 0.001$), and disease control ($P = 0.02$). Eradication of the infection was successful in 77/101 (76.2%) of the patients on intent-to-treat analysis and 77/94 (81.9%) on per-protocol analysis. Eradication was associated with an increase in mean (SD) QOL score to 70.8 (10.7) at 6 weeks (95% CI, 63.3–73.2; $P < 0.001$ vs baseline) and to 75.3 (9.3) at 1 year (95% CI, 73.2–77.5; $P = 0.05$ vs 6 weeks). In the HP– group, the QOL score increased to 73.3 (9.7) (95% CI, 71.3–75.4; $P < 0.001$ vs baseline) at 6 weeks of cisapride treatment and to 76.5 (8.5) at 1 year (95% CI, 74.5–78.4; $P = 0.06$ vs 6 weeks). Most of the impaired domain scores improved significantly after both treatments. The short-term effect size was 1.48 in HP+ and 1.35 in HP– patients. Adverse events (AEs) occurred in 22 (21.8%) patients in the HP+ group (nausea, 8 [7.9%] patients; diarrhea, 5 [5.0%]; loss of appetite, 5 [5.0%]; stomatitis, 5 [5.0%]; abdominal pain, 4 [4.0%]; bloating, 4 [4.0%]; headache, 4 [4.0%]; vomiting, 4 [4.0%]; constipation, 3 [3.0%]; and vaginitis, 3 [3.0%]). In HP– cases, AEs occurred in 9 (9.2%) patients (abdominal cramps, 7 [7.1%]; diarrhea, 4 [4.1%]; and nausea, 3 [3.1%]).

Conclusion: In this study in patients with FD and healthy controls, eradication of *H pylori* infection in infected patients and cisapride treatment in uninfected patients reversed low QOL scores during the 1-year follow-up period. (*Curr Ther Res Clin Exp.* 2006;67:305–320) Copyright © 2006 Excerpta Medica, Inc.

Key words: eradication, functional dyspepsia, *Helicobacter pylori*, prokinetics, quality of life.

INTRODUCTION

Dyspepsia has a prevalence of 25% in Western countries. Despite the many attempts to define the disease, it remains a poorly defined, misunderstood condition.[1] In Europe, the Rome II criteria have been used in clinical trials of antidyspepsia treatments.[2] Most dyspeptic patients do not have structural abnormalities that account for their symptoms and thus are considered to have functional dyspepsia (FD). While FD has not been associated with mortality and complications, an outcome assessment using quality-of-life (QOL) instruments is recommended in these patients.

In the past, the results of drug treatment trials in FD may have been biased by the variability of the inclusion criteria, the heterogeneity of FD (ulcerlike, dysmotility-like, or mixed types), the high rate of placebo response (40%–70%), and differences in outcomes evaluations (symptom grading or general or disease-specific QOL instruments). The results may also have varied according to the research setting; disease severity and treatment outcomes may have differed in patients treated as secondary or tertiary referrals compared with those treated in a primary care setting.[1] *Helicobacter pylori* is encountered in 30% to 50% of individuals with FD, but

its pathogenetic implications are far from clear, and evidence of the benefits of eradication is equivocal.[1,2]

The aims of this study were to measure baseline QOL in patients with FD and to assess changes in QOL over time associated with *H pylori* eradication and prokinetic treatment. The primary and secondary end points were the improvement in QOL 6 weeks and 1 year after successful eradication of the infection or prokinetic therapy. Because mortality and complications are unusual in patients with FD, the assessment of QOL was used as the measure of the outcome and primary and secondary end points.

PATIENTS AND METHODS

Study Design

This 1-year, single-center, prospective, open-label, controlled, parallel-group trial was conducted at the Department of Gastroenterology, Ferencváros Health Centre, Budapest, Hungary. The study protocol was approved by the local ethics committee and conformed to the principles in the Declaration of Helsinki and its amendments.[3]

Study Population

Male and female *H pylori*–positive (HP+) and *H pylori*–negative (HP–) patients with FD and healthy subjects (control) were enrolled. The inclusion criteria were age between 20 and 60 years and the presence of dyspepsia according to the Rome II criteria.[2] Patients were excluded if they had any other chronic organic diseases that could alter QOL and that required drug treatment (eg, severe hypertension, myocardial ischemia/infarction, congestive heart failure, diabetes mellitus, renal failure, cirrhosis, previous gastric surgery [resection, vagotomy], biliary stone disease, chronic pancreatitis, chronic obstructive pulmonary disease, rheumatoid arthritis, heavy drinking [>5 alcoholic beverages/d]) or regular use of nonsteroidal anti-inflammatory drugs (eg, acetylsalicylic acid, naproxen, indomethacin, diclofenac, celecoxib, meloxicam, nabumetone) or bisphosphonates (eg, alendronate).

In dyspeptic patients, organic diseases were ruled out using endoscopy (Fujinon UGI FP7, Fuji Photo Optical Co. Ltd., Saitasma, Japan) and abdominal ultrasonography (Sonoline Prima, Siemens AG, Munich, Germany). The diagnosis of *H pylori* infection was confirmed on biopsy using modified Giemsa stain and a rapid urease test (Controloc Test kit, Byk-Gulden [now ALTANA Pharma AG], Konstanz, Germany). HP– patients were not retested using any other method (eg, serology, breath test).

Healthy controls were enrolled from among individuals referred by Dimension Insurance Ltd., Budapest, Hungary, which conducts biennial fee-for-service gastroenterologic screening consisting of a medical history, physical examination, abdominal ultrasonography, and basic laboratory studies (complete blood count, glucose concentration, lipid profile, kidney function, C-reactive protein,

and liver enzymes). The controls were not tested for *H pylori* before inclusion in the QOL study.

QOL was assessed using the Functional Digestive Disorders Quality of Life (FDDQoL) Questionnaire developed by the MAPI Research Institute (Lyon, France)[4] and translated and validated in Hungarian[5] to have psychometric properties similar to those of the original version. The questionnaire includes 43 items organized in 8 domains: daily activities (8 items), anxiety level (5), diet (6), sleep (3), discomfort (9), coping with disease (6), disease control (3), and the influence of stress (3). Answer options comprised 5- and 6-point Likert scales. The questionnaire was self-administered to all participants at baseline and at 6 weeks and 1 year after *H pylori* eradication or cisapride therapy.

Written informed consent was obtained from all participants. Three visits (baseline, 6 weeks, and 1 year) were required for the dyspeptic patients and 1 visit (baseline) for the controls.

Study Drug Administration

The study design is shown in **Figure 1**.

All drugs in this study were self-administered as tablets. HP+ patients received pantoprazole 40 mg BID + amoxicillin 1000 mg BID + clarithromycin 500 mg BID for 7 days, followed by on-demand ranitidine 150–300 mg/d during the 1-year follow-up period. A control ^{13}C-urea breath test using isotope-selective infrared spectrometry (IRIS C13, Wagner Analysentechnik GmbH, Bremen, Germany) was performed 6 weeks after eradication. The patients were blinded to the results of their eradication status before they completed the questionnaire. HP– patients received cisapride 10 mg TID for 1 month followed by on-demand cisapride 10–20 mg/d for 1 year. Compliance was assessed using a pill count during the short-term treatment and by self-reporting during the maintenance period. Ranitidine or cisapride use (mg/wk) was estimated based on patients' reports.

Statistical Analysis

A sample size of 78 patients in each group was calculated for a power of 80% to detect a 15% difference between groups. The raw scores were calculated. After standardization and linear transformation of the raw scores (STSs), a scale of 0 to 100 points was obtained (the higher the value, the better the QOL). The normal range of the STS QOL scores was defined as the mean (SD) of the values found in the healthy controls. The 95% CIs were determined for the STS scores. Differences between the groups and the change over time in both groups of patients with FD were calculated using analysis of variance (ANOVA), and P values <0.05 were considered significant. The post-hoc Tukey test was used when appropriate. Differences in QOL domain scores were also assessed using ANOVA. The influence of demographic variables on QOL was assessed using multiple logistic regression analysis. Eradication results were expressed

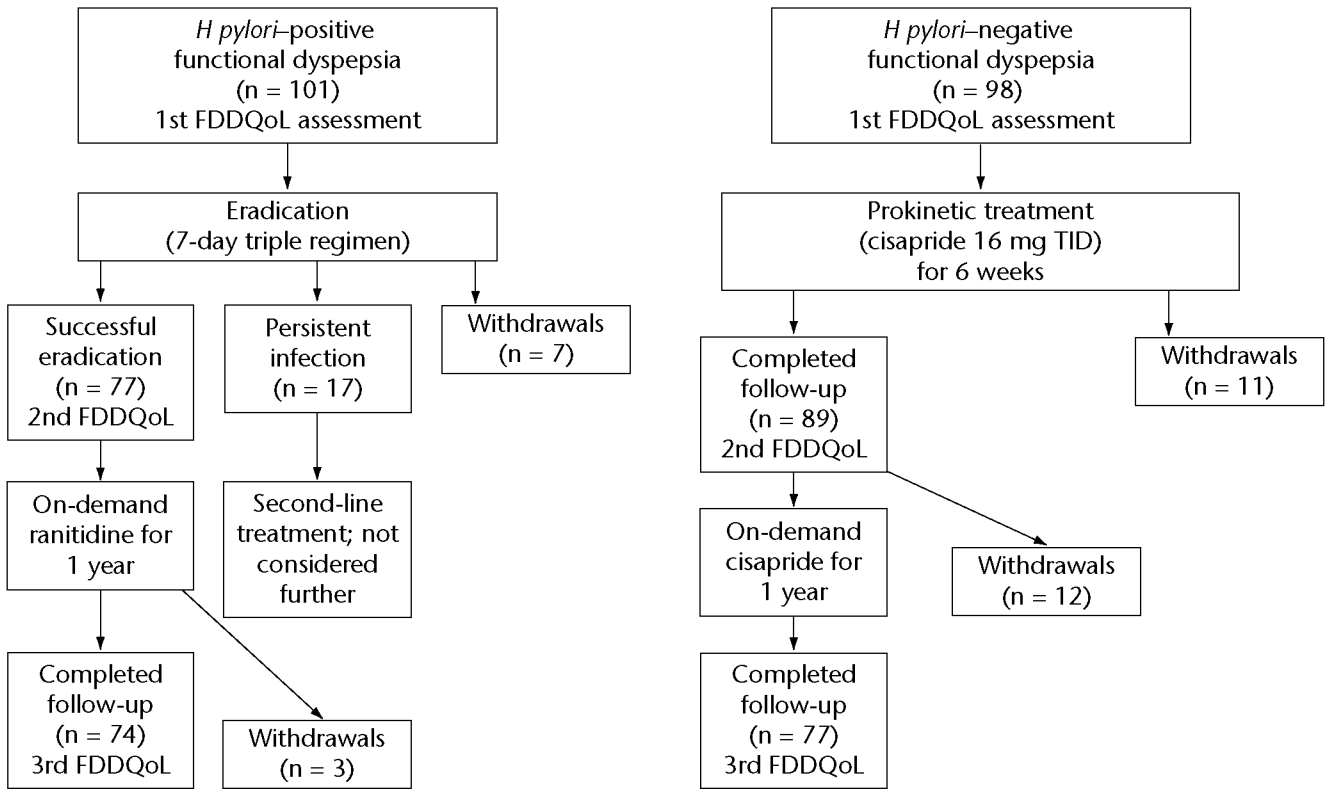

Figure 1. Study design. ***H pylori*** **=** ***Helicobacter pylori*****; FDDQoL = Functional Digestive Disorders Quality of Life Questionnaire.**[4]

on intent-to-treat (ITT) and per-protocol (PP) bases. For items that were missing or not applicable, case regression imputation was used as appropriate; for missing questionnaires, simple mean imputation was performed. The effect size was defined as the difference between the mean score of the week-6 and baseline QOL assessments divided by the SD of the baseline measurement.[6] Between-group differences were calculated using the 2-tailed *t* test.[6] The statistics were calculated using Statistica version 9.0 (StatSoft, Inc., Tulsa, Oklahoma).

RESULTS

A total of 101 HP+ patients, 98 HP– patients with FD, and 123 healthy controls were included in the study (185 women, 137 men; mean age, 39.0 years). The baseline demographic data for the 3 groups are given in **Table I**.

The mean (SD) baseline STS QOL scores were significantly lower in the HP+ group (53.3 [9.6]; 95% CI, 54.4–58.2) and HP– group (50.0 [9.8]; 95% CI, 58.0–62.0) compared with that in the healthy controls (76.2 [8.7]; 95% CI, 74.6–77.8) (both, $P < 0.001$) (**Table II** and **Figure 2**). The normal STS QOL range (70.9–81.5) was the value found in the healthy controls. The baseline QOL domain values are shown in **Table II**.

Effects of Eradication Therapy on Quality of Life

H pylori was eradicated in 77/101 (76.2%) of patients on ITT analysis and 77/94 (81.9%) on PP analysis. In successfully treated cases, the mean (SD) STS QOL scores increased from 56.2 (9.8) (95% CI, 53.9–58.4) to 70.8 (10.7) (95% CI, 63.3–73.2) at 6 weeks ($P < 0.001$ vs baseline) and to 75.3 (9.3) (95% CI, 73.2–77.5)

Table I. Baseline demographic and clinical characteristics of the study population (N = 322).*

Characteristic	HP+ (n = 101)	HP– (n = 98)	Control (n = 123)
Age, y			
Mean (SD)	38.6 (11.6)	39.3 (12.4)	39.2 (11.0)
Range	18–72	20–67	21–64
Sex, no. (%)			
Female	67 (66.3)	62 (63.3)	56 (45.5)
Male	34 (33.7)	36 (36.7)	67 (54.5)
Disease duration of complaints, mean (SD), y	3.4 (3.4)	3.2 (3.7)	–
Smoking, no (%)	50 (49.5)	49 (50.5)	34 (27.6)
Alcohol use, no (%)†	20 (19.8)	14 (14.3)	19 (15.4)

HP+ = *Helicobacter pylori* positive; HP– = *Helicobacter pylori* negative.
*No significant between-group differences were found.
†Heavy drinkers (>5 alcoholic beverages/d) were excluded from the study.

Table II. Baseline distribution of the domain scores on the Functional Digestive Disorders Quality of Life (QOL) Questionnaire[4]* in patients with *Helicobacter pylori*–positive (HP+) and –negative (HP–) functional dyspepsia and healthy subjects (control). Data are mean standardized scores after linear transformation (95% CI).

QOL Domain	HP+ (n = 101)	HP– (n = 98)	Control (n = 123)
Daily activities	54.6 (50.6–58.5)†	54.9 (51.4–58.4)†	79.9 (77.1–82.1)
Anxiety level	51.8 (48.1–55.5)‡	49.9 (46.7–53.3)§	67.7 (65.0–70.4)
Diet	53.7 (50.9–56.7)†	56.6 (53.5–59.7)†	70.8 (68.6–73.2)
Sleep	55.3 (49.6–63.0)†	56.6 (54.0–59.1)†	64.9 (64.1–65.8)
Discomfort	51.2 (48.6–53.7)†	55.3 (52.5–58.1)†	63.7 (61.5–65.9)
Coping with disease	45.4 (42.6–48.2)	46.4 (43.7–49.0)	46.5 (44.0–49.0)
Disease control	53.9 (51.1–56.9)†	51.5 (48.4–54.7)†	59.7 (57.4–61.9)
Stress	56.3 (54.4–58.2)	50.2 (47.1–53.3)†	56.4 (53.8–58.9)
Global scores‖	53.3 (9.6) (54.4–58.2)†	50.0 (9.8) (58.0–62.0)†	76.2 (8.7) (74.6–77.8)

*The questionnaire scale includes 43 items organized in 8 domains: daily activities (8 items), anxiety level (5), diet (6), sleep (3), discomfort (9), coping with disease (6), disease control (3), and the influence of stress (3). Answer options comprise 5- and 6-point Likert scales.
†$P < 0.001$ versus controls.
‡$P = 0.011$ versus controls.
§$P = 0.022$ versus controls.
‖Mean (SD) (95% CI).

at 1 year ($P = 0.05$ vs 6 weeks) (**Figure 3**). In patients with persistent infection, the STS QOL scores were 53.3 (95% CI, 54.4–58.2) at baseline and 56.0 (95% CI, 49.9–62.1) at 6 weeks. These patients underwent second- and third-line therapies and were not considered for analysis at 1 year.

The changes over time in the domain scores are shown in **Table III**. Analysis of the domain scores found that FD was associated with impairment of almost all domains of QOL (ie, daily activities, anxiety level, diet, sleep, discomfort, disease control, and stress). There was no significant difference in the domain of coping with FD. The profile of QOL impairment and its reversal after treatment was similar between the HP+ and HP– patients; the HP+ group had significantly

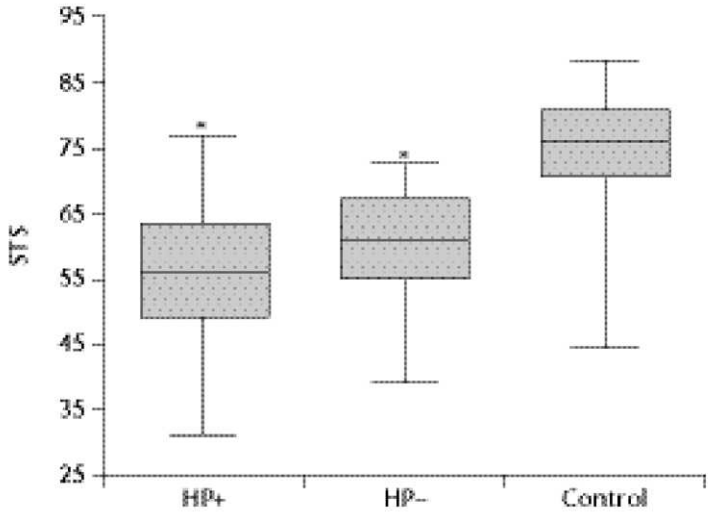

Figure 2. Median (25%–75%) standardized and linear-transformed scores (STS) for quality of life in patients with *Helicobacter pylori*–positive (HP+) and –negative (HP–) functional dyspepsia and healthy controls. *$P < 0.001$ versus control.

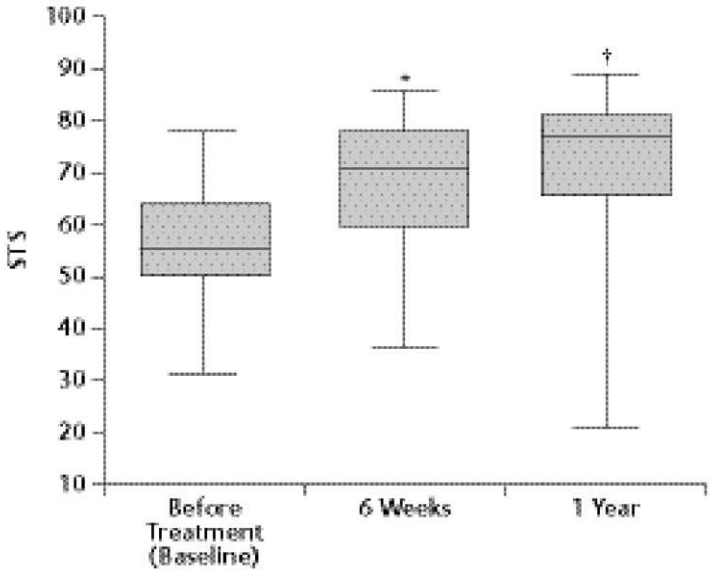

Figure 3. Median (25%–75%) standardized and linear-transformed scores (STS) for quality of life after *Helicobacter pylori* eradication in patients with functional dyspepsia. *$P < 0.001$ versus baseline; †$P = 0.05$ versus 6 weeks.

Table III. Distribution of the domain scores for the Functional Digestive Disorders Quality of Life (QOL) Questionnaire[4]* in patients with *Helicobacter pylori*–positive (HP+) and –negative (HP–) functional dyspepsia after successful eradication or prokinetic treatment at baseline and at 6 weeks and 1 year. Data are mean standardized scores after linear transformation.

	HP+					HP–				
QOL Domain	Baseline	6 Weeks	*P* Versus Baseline	HP+ 1 Year	*P* Versus Baseline	Baseline	6 Weeks	*P* Versus Baseline	HP– 1 Year	*P* Versus Baseline
Daily activities	54.6	66.8	0.005	67.3	0.99	54.7	74.5	<0.001	76.2	0.99
Anxiety level	51.8	59.2	0.02	58.7	0.99	49.9	59.9	0.06	63.5	0.82
Diet	53.7	62.0	0.008	64.8	0.96	56.6	62.7	0.004	66.6	0.73
Sleep	55.3	61.6	<0.001	61.7	0.99	56.6	62.1	0.005	64.7	0.65
Discomfort	51.2	59.4	0.004	61.7	0.96	55.3	64.5	<0.001	64.6	0.99
Coping with disease	45.4	48.6	0.12	48.6	0.14	46.4	48.6	0.32	60.7	0.31
Disease control	53.9	58.6	0.02	53.3	0.01	51.5	56.4	0.02	55.1	0.56
Stress	50.2	53.3	0.13	54.0	0.73	50.2	52.6	0.27	54.9	0.04

*The questionnaire includes 43 items organized in 8 domains: daily activities (8 items), anxiety level (5), diet (6), sleep (3), discomfort (9), coping with disease (6), disease control (3), and the influence of stress (3). Answer options comprise 5- and 6-point Likert scales.

decreased scores in 6 of 8 domains: daily activities ($P = 0.005$), anxiety level ($P = 0.02$), diet ($P = 0.008$), sleep ($P < 0.001$), discomfort ($P = 0.004$), and disease control ($P = 0.02$); the HP– group had significantly decreased scores in 5 of 8 domains: daily activities ($P < 0.001$), diet ($P = 0.004$), sleep ($P = 0.005$), discomfort ($P < 0.001$), and disease control ($P = 0.02$). At 1-year follow-up, only disease control increased significantly in HP+ patients, and stress in HP– patients.

The compliance rate was 88% at 6 weeks and 74% at 1 year. During the follow-up period, the mean dose of ranitidine was 150 mg TIW.

The short-term effect size was 1.48 in HP+ and 1.35 in HP– patients (**Table IV**).

Effects of Cisapride on Quality of Life

In the HP– group, mean (SD) STS QOL increased from 50.0 (9.8) (95% CI, 58.0–62.0) at baseline to 73.3 (9.7) (95% CI, 71.3–75.4) at 6 weeks of cisapride treatment ($P < 0.001$) and to 76.5 (8.5) (95% CI, 74.5–78.4) at 1 year ($P = 0.06$ vs 6 weeks) (**Figure 4**).

The changes over time in the domain scores are shown in **Table III**.

The compliance rate was 92% at 6 weeks and 78% at 1 year. During the follow-up period, the mean dose of cisapride was 40 mg/wk.

The effect size was large after short-term therapy and small during maintenance treatment (**Table IV**).

Multiple logistic regression analysis showed that increasing age ($r = 0.30$; $P = 0.07$) and female sex ($r = 0.23$; $P = 0.04$) were associated with QOL in HP– patients with FD at baseline; after cisapride therapy, only age was associated with QOL ($r = 0.38$; $P = 0.01$). No such effect was observed in HP+ patients. Smoking, alcohol consumption, and duration of complaints were not associated with changes in QOL before or after treatment in either group.

Tolerability

Adverse events (AEs) occurred in 22 (21.8%) patients in the HP+ group (nausea, 8 [7.9%] patients; diarrhea, 5 [5.0%]; loss of appetite, 5 [5.0%]; stomatitis, 5 [5.0%]; abdominal pain, 4 [4.0%]; bloating, 4 [4.0%]; headache, 4 [4.0%]; vomit-

Table IV. Effect size of *Helicobacter pylori* eradication and cisapride treatment in patients with functional dyspepsia.*

Group	n	Effect Size
HP+	101	
Short-term successful eradication	82	1.48
On-demand ranitidine for 1 year	74	0.68
HP–	98	
Short-term cisapride therapy	93	1.35
On-demand cisapride for 1 year	77	0.34

HP+ = *Helicobacter pylori* positive; HP– = *Helicobacter pylori* negative.
*No significant between-group differences were found.

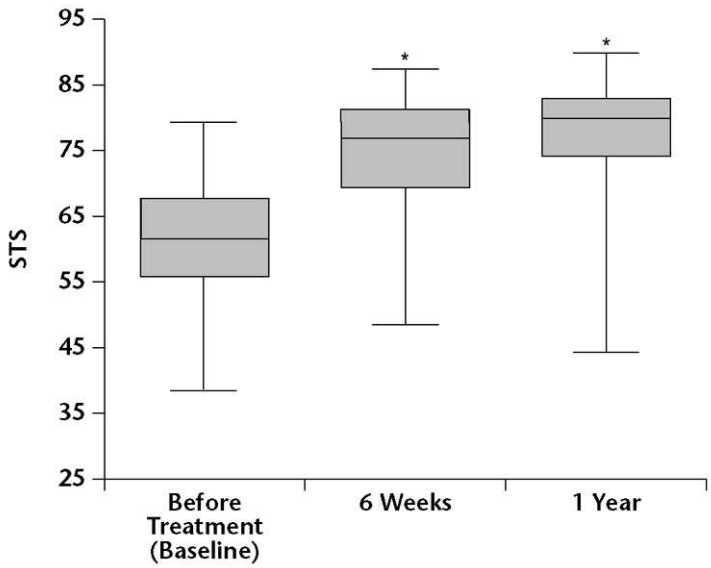

Figure 4. Median (25%–75%) standardized and linear-transformed scores (STS) for quality of life in *Helicobacter pylori*–negative patients with functional dyspepsia receiving cisapride treatment. *$P < 0.001$ versus baseline.

ing, 4 [4.0%]; constipation, 3 [3.0%]; and vaginitis, 3 [3.0%]). In the HP– group, AEs occurred in 9 (9.2%) patients (abdominal cramps, 7 [7.1%]; diarrhea, 4 [4.1%]; and nausea, 3 [3.1%]). No cardiac AEs were reported in either group. One HP+ patients and 2 HP– patients discontinued treatment because of vaginitis and severe diarrhea, respectively.

DISCUSSION

Several disease-specific QOL instruments have been developed,[7–12] but all have some methodologic flaws.[13,14] The FDDQoL has acceptable reliability and validity, but its sensitivity to capture treatment effects has been found only in irritable bowel disease.[4]

QOL has been found to be impaired in some patients with FD.[1,4,7–12] The degree of functional impairment is similar to or more severe than in organic diseases (eg, ulcer, reflux disease).[11] Subtypes of FD may be associated with different patterns and/or severity of impairment.[11] The results of the present study suggest that QOL is impaired in patients with FD compared with healthy controls. Because only investigated cases were included, the patients in the present study did not represent the entire dyspeptic population. It was not possible to distinguish patients with and without *H pylori* infection based on QOL data, which is supported by the findings in a previous clinical study.[15]

The isolated improvements in QOL domains—disease control in HP+ patients and stress in HP– patients—found at 1-year follow-up are difficult to explain. Demographic variables (age and female sex) had a modest influence on QOL in HP– patients with FD. Impairment might have been caused by the dyspeptic symptoms themselves and not by other factors (eg, smoking, alcohol consumption).

The European consensus report[16] on the management of *H pylori* infection recommends eradication of *H pylori* in individuals with FD after a full investigation. Meta-analyses of clinical trials in patients with FD have found that eradication was associated with a minor improvement in dyspeptic symptoms.[17,18] Other studies, however, have found variable levels of symptomatic relief and improvement in QOL in subgroups of FD patients.[19–22] In primary care settings, eradication of *H pylori* improved symptoms and QOL in Canadian,[23,24] British,[25] Finnish,[26] and Japanese populations,[27,28] and was found to be cost-effective in Canada and the United Kingdom.[24,29] Lack of benefit of eradicating the infection in patients with FD was reported in the United Kingdom,[29] Spain,[30] Denmark,[31] and Mexico.[32] The use of different QOL instruments in different populations might explain the divergent findings.

In the present study, *H pylori* eradication was associated with significant improvements in short- and long-term QOL (7 of 8 domains) and in dyspeptic symptoms. The effect size was large after 6 weeks; on-demand maintenance treatment did not add to the 1-year improvement in QOL. Some arguments favor the eradication policy (eg, the prevention of subsequent occurrences of peptic ulcer/gastric cancer, decreases in the prevalence of the infection and the infectious reservoir of the population). One-week triple therapy achieved a high rate of eradication, as suggested by international standards.[16] FD is a chronic, recurrent disorder, and follow-up lasting >1 year may be needed before declaring a definitive improvement in QOL after eradication. Studies of long-term follow-up of 5 years in 100 cases and 7 years in 201 patients with FD found either symptomatic resolution and prevention of disease progression[33,34] or persistence of dyspepsia over a long period after *H pylori* eradication.[35] We plan to follow up the patients in the present study for 3 to 5 years, with the results expected in 2007 or 2008.

Two studies have found a favorable effect of cisapride in FD.[36,37] However, symptom improvement was variable, and the results in patients recruited from primary care were negative.[1,2] In a recent systematic review, prokinetics were found to be superior to placebo for FD therapy,[38] but only a limited number of agents of this class can currently be prescribed.[39] Studies assessing QOL in patients with FD who are receiving prokinetic therapy are scarce. In 1 such study, in which symptom severity and QOL were improved after 1 year of cisapride therapy in 57 patients with FD, only generic instruments were used.[40] In a randomized trial in 512 patients with FD, symptom relief was significantly improved with omeprazole compared with cisapride, ranitidine, and placebo; however, no QOL assessment was undertaken.[41] None of these studies determined whether the prokinetic effect was dependent on *H pylori* status.

This study supports the short- and long-term benefits of cisapride treatment in HP– patients with FD. The effect size of prokinetic therapy was large after short-term and small after maintenance therapy. However, the favorable results are overshadowed by the proarrhythmic AE of cisapride[42]; for this reason, the drug was withdrawn from the markets in Europe and the United States. FDDQoL is a valuable instrument for assessing QOL and might be used in the future for the evaluation of emergent prokinetic therapies. For instance, in an Australian study in 554 patients with FD, dyspeptic symptoms were more improved with the dopamine D2 receptor antagonist itopride compared with placebo.[43]

The present study had some limitations. Because the study was performed in clinical practice, the inclusion of a placebo or untreated HP+ or HP– control group during the active phase of the trial was considered unethical and would have violated the European and the Hungarian consensus statements.[16,44] In addition, the study was not randomized because the patients were included in the HP+ or HP– group a priori.

Even with these limitations, the results support a QOL benefit of eradicating *H pylori* in patients with FD. Prokinetic treatment also proved to be useful for improving QOL in HP– patients with FD.

Nonetheless, FD treatment has some unresolved caveats; the optimal therapy is still unclear. New pathogenetic hypotheses are arising and a better understanding of abnormalities underlying FD may lead to improved disease management.[45–47] We believe that assessment of QOL will have a place in the evaluation of novel therapies.

CONCLUSIONS

In this study in patients with FD, eradication of *H pylori* infection in infected patients and cisapride treatment in uninfected patients reversed low QOL scores and improved global QOL during the 1-year follow-up period.

ACKNOWLEDGMENTS

The administrative and statistical help of Jolán Józan (National Institute of Traumatology, Department of Experimental Medicine, Budapest, Hungary) is appreciated. The author thanks Douglas Arnott (EDMF Translation Bureau BT, Budapest, Hungary) for reviewing the English manuscript.

REFERENCES

1. Bytzer P, Talley NJ. Dyspepsia. *Ann Intern Med.* 2001;134:815–822.
2. Talley NJ, Stanghellini V, Heading RC, et al. Functional gastroduodenal disorders. *Gut.* 1999;45(Suppl 2):II37–II42.
3. World Medical Association Declaration of Helsinki: Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects [WMA Web site].

Ferney-Voltaire, France: WMA; 1989. Available at: http://www.wma.net. Accessed June 15, 2005.

4. Chassany O, Marquis P, Scherrer B, et al. Validation of a specific quality of life questionnaire for functional digestive disorders. *Gut.* 1999;44:527–533.
5. Buzás GM. Assessment of quality of life in functional dyspepsia. Validation of a questionnaire and its use in clinical practice [in Hungarian]. *Orv Hetil.* 2004;145:687–692.
6. Fayers PM, Machin D, eds. *Quality of Life: Assessment, Analysis and Interpretation.* Chichester, UK: John Wiley & Sons; 2000.
7. el-Omar EM, Banerjee S, Wirz A, McColl KE. The Glasgow Dyspepsia Severity Score—a tool for the global measurement of dyspepsia. *Eur J Gastroenterol Hepatol.* 1996;8: 967–971.
8. Cook KF, Rabeneck L, Campbell CJ, Wray NP. Evaluation of a multidimensional measure of dyspepsia-related health for use in a randomized clinical trial. *J Clin Epidemiol.* 1999;52:381–392.
9. Wiklund IK, Junghard O, Grace E, et al. Quality of life in reflux and dyspepsia patients. Psychometric documentation of a new disease-specific questionnaire (QOLRAD). *Eur J Surg Suppl.* 1998;583:41–49.
10. Leidy NK, Farup C, Rentz AM, et al. Patient-based assessment in dyspepsia: Development and validation of Dyspepsia Symptoms Severity Score Index (DSSI). *Dig Dis Sci.* 2000;45:1172–1179.
11. Talley NJ, Verlinden M, Jones M. Validity of a new quality of life scale for functional dyspepsia: A United States multicenter trial of the Nepean Dyspepsia Index. *Am J Gastroenterol.* 1999;94:2390–2397.
12. Mones J, Adan A, Segu JL, et al. Quality of life in functional dyspepsia. *Dig Dis Sci.* 2002;47:20–26.
13. Rentz AM, Battista C, Trudeau E, et al. Symptom and health-related quality-of-life measures for use in selected gastrointestinal disease studies: A review and synthesis of the literature. *PharmacoEconomics.* 2001;19:349–363.
14. Yacavone RF, Locke GR III, Provenzale DT, Eisen GM. Quality of life measurement in gastroenterology: What is available? *Am J Gastroenterol.* 2001;96:285–297.
15. Werdmüller BF, van der Putten TB, Balk TG, et al. Clinical presentation of *Helicobacter pylori*–positive and –negative functional dyspepsia. *J Gastroenterol Hepatol.* 2000;15:498–502.
16. Malfertheiner P, Megraud F, O'Morain C, et al, for the European *Helicobacter pylori* Study Group (EHPSG). Current concepts in the management of *Helicobacter pylori* infection—the Maastricht 2-2000 Consensus Report. *Aliment Pharmacol Ther.* 2002;16:167–180.
17. Laine L, Schoenfeld P, Fennerty MB. Therapy for *Helicobacter pylori* in patients with nonulcer dyspepsia. A meta-analysis of randomized, controlled trials. *Ann Intern Med.* 2001;134:361–369.
18. Jaakkimainen RL, Boyle E, Tudiver F. Is *Helicobacter pylori* associated with non-ulcer dyspepsia and will eradication improve symptoms? A meta-analysis. *BMJ.* 1999;319: 1040–1044.
19. Froehlich F, Gonvers JJ, Wietlisbach V, et al, for the Eradication in Dyspepsia (ERADYS) Study Group. *Helicobacter pylori* eradication treatment does not benefit patients with nonulcer dyspepsia. *Am J Gastroenterol.* 2001;96:2329–2336.
20. Moayyedi P, Feltbower R, Brown J, et al, for the Leeds HELP Study Group. Effect of population screening and treatment for *Helicobacter pylori* on dyspepsia and quality of life in the community: A randomised controlled trial. *Lancet.* 2000;355:1665–1669.

21. McColl K, Murray L, El-Omar E, et al. Symptomatic benefit from eradicating *Helicobacter pylori* infection in patients with nonulcer dyspepsia. *N Engl J Med.* 1998;339:1869–1874.
22. Bruley des Varannes S, Flejou JF, Colin R, et al. There are some benefits for eradicating *Helicobacter pylori* in patients with non-ulcer dyspepsia. *Aliment Pharmacol Ther.* 2001;15:1177–1185.
23. Chiba N, van Zanten SJ, Sinclair P, et al. Treating *Helicobacter pylori* infection in primary care patients with uninvestigated dyspepsia: The Canadian adult dyspepsia empiric treatment-*Helicobacter pylori* positive (CADET-Hp) randomised controlled trial. *BMJ.* 2002;324:1012–1016.
24. Chiba N, Veldhuyzen van Zanten SJ, Escobedo S, et al. Economic evaluation of *Helicobacter pylori* eradication in the CADET-Hp randomized controlled trial of *H. pylori*–positive primary care patients with uninvestigated dyspepsia. *Aliment Pharmacol Ther.* 2004;19:349–358.
25. Verma S, Giaffer MH. *Helicobacter pylori* eradication ameliorates symptoms and improves quality of life in patients on long-term acid suppression. A large prospective study in primary care. *Dig Dis Sci.* 2002;47:1567–1574.
26. Farkkila M, Sarna S, Valtonen V, Sipponen P, for the PROSPER Study Group. Does the 'test-and-treat' strategy work in primary health care for management of uninvestigated dyspepsia? A prospective two-year follow-up study of 1552 patients. *Scand J Gastroenterol.* 2004;39:327–335.
27. Fujiwara Y, Higuchi K, Arafa UA, et al. Long-term effect of *Helicobacter pylori* eradication on quality of life, body mass index, and newly developed diseases in Japanese patients with peptic ulcer disease. *Hepatogastroenterology.* 2002;49:1298–1302.
28. Suzuki H, Masaoka T, Sakai G, et al. Improvement of gastrointestinal quality of life scores in cases of *Helicobacter pylori*–positive functional dyspepsia after successful eradication therapy. *J Gastroenterol Hepatol.* 2005;20:1652–1660.
29. Lane JA, Murray LJ, Noble S, et al. Impact of *Helicobacter pylori* eradication on dyspepsia, health resource use, and quality of life in the Bristol *Helicobacter* project: Randomised controlled trial. *BMJ.* 2006:332;199–204.
30. Gisbert JP, Cruzado AI, Garcia-Gravalos R, Pajares JM. Lack of benefit of treating *Helicobacter pylori* infection in patients with functional dyspepsia. Randomized one-year follow-up study. *Hepatogastroenterology.* 2004;51:303–308.
31. Wildner-Christensen M, Moller Hansen J, Schaffalitzky De Muckadell OB. Rates of dyspepsia one year after *Helicobacter pylori* screening and eradication in a Danish population. *Gastroenterology.* 2003;125:372–379.
32. Ladron de Guevara L, Pena-Alfaro NG, Padilla L, et al. Evaluation of the symptomatology and quality of life in functional dyspepsia before and after *Helicobacter pylori* eradication treatment [in Spanish]. *Rev Gastroenterol Mex.* 2004;69:203–308.
33. McNamara D, Buckley M, Gilvarry J, O'Morain C. Does *Helicobacter pylori* eradication affect symptoms in nonulcer dyspepsia: A 5-year follow-up study. *Helicobacter.* 2002; 7:317–321.
34. Heikkinen M, Farkkila M. Long-term outcome of functional dyspepsia: Effect of *Helicobacter pylori* infection. A 6- to 7-year follow-up study. *Scand J Gastroenterol.* 2002;37:905–910.
35. di Mario F, Stefani N, Bo ND, et al. Natural course of functional dyspepsia after *Helicobacter pylori* eradication: A seven-year survey. *Dig Dis Sci.* 2005;50:2286–2295.

36. Finney JS, Kinnersley N, Hughes M, et al. Meta-analysis of antisecretory and gastrokinetic compounds in functional dyspepsia. *J Clin Gastroenterol.* 1998;26:312–320.
37. Veldhuyzen van Zanten SJ, Jones MJ, Verlinden M, Talley NJ. Efficacy of cisapride and domperidone in functional (nonulcer) dyspepsia: A meta-analysis. *Am J Gastroenterol.* 2001;96:689–696.
38. Moayyedi P, Soo S, Deeks J, et al. Systematic review: Antacids, H2-receptor antagonists, prokinetics, bismuth and sucralfate therapy for non-ulcer dyspepsia. *Aliment Pharmacol Ther.* 2003;17:1215–1227.
39. Talley NJ. Update on the role of drug therapy in non-ulcer dyspepsia. *Rev Gastroenterol Disord.* 2003;3:25–30.
40. Cutts TF, Abell TL, Karas JG, Kuns J. Symptom improvement from prokinetic therapy corresponds to improved quality of life in patients with severe dyspepsia. *Dig Dis Sci.* 1996;41:1369–1378.
41. Veldhuyzen van Zanten SJ, Chiba N, Armstrong D, et al. A randomized trial comparing omeprazole, ranitidine, cisapride, or placebo in *Helicobacter pylori* negative, primary care patients with dyspepsia: The CADET-HN Study. *Am J Gastroenterol.* 2005;100:1477–1488.
42. Elming H, Sonne J, Lublin HK. The importance of the QT interval: A review of the literature. *Acta Psychiatr Scand.* 2003;107:96–101.
43. Holtmann G, Talley NJ, Liebregts T, et al. A placebo-controlled trial of itopride in functional dyspepsia [published correction appears in *N Engl J Med.* 2006;355:429]. *N Engl J Med.* 2006;354:832–840.
44. Rácz I, Bajtai A, Lonovics J, Simon L. The treatment of *Helicobacter pylori* infection. *Eur J Gastroenterol Hepatol (Hungarian edition).* 2000;4:145–154.
45. Madisch A, Miehlke S, Labenz J. Management of functional dyspepsia: Unsolved problems and new perspectives. *World J Gastroenterol.* 2005;11:6577–6581.
46. Choung RS, Talley NJ. Novel mechanisms in functional dyspepsia. *World J Gastroenterol.* 2006;12:673–677.
47. Holtmann G, Talley NJ. Hypothesis driven research and molecular mechanisms in functional dyspepsia: The beginning of a beautiful friendship in research and practice? *Am J Gastroenterol.* 2006;101:593–595.

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