Functional dyspepsia symptom resolution after *Helicobacter pylori* eradication with two different regimens

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Abstract

Introduction: Functional dyspepsia (FD), a common functional gastrointestinal disorder, has a complex underlying pathophysiological mechanism that involves changes in gastric motility, visceral hypersensitivity, genetic susceptibility, psychosocial factors and *Helicobacter pylori* infection. Although there are several *H. pylori* eradication treatments, there is not enough data that compare these different eradication treatments for FD symptom resolution. Most previous studies have focused on the eradication rates of *H. pylori* rather than symptom relief in FD.

Aim: In this regard, we aimed to clarify if there is any difference between standard triple therapy and sequential therapy for symptom resolution of FD patients with *H. pylori*, using a validated health quality index.

Material and methods: A total of 194 patients were included in this study. The patients were randomly assigned to receive standard triple therapy (omeprazole, amoxicilline and clarithromycin for 14 days) or sequential therapy (omeprazole plus amoxicilline for 7 days and omeprazole twice daily, metronidazole and clarithromycin for a subsequent 7 days) by a blind physician for *H. pylori* status. Outcome measures were based on symptomatic improvement at 12 months using a validated measure of subjective well-being (Gastrointestinal Symptom Rating Scale – GSRS).

Results: We observed significant symptom resolution at 12 months in both treatment groups. On the other hand, there was no difference between the sequential or standard triple therapy groups regarding the alleviation of symptoms.

Conclusions: No difference for symptom relief exists between sequential and triple therapy in patients with FD.

Introduction

Dyspepsia is one of the most common chronic illnesses of adults and affects up to 40% of the population in the Western world [1]. Not surprisingly, the cost of dyspepsia treatment represents a large proportion of the healthcare expenses in developed countries [2]. Similarly, dyspepsia affects 28.4% of the population in Turkey, and the majority of them take medications for dyspepsia [3].

Functional dyspepsia (FD), a common functional gastrointestinal disorder, is defined by the Rome III criteria as symptoms of epigastric pain or discomfort, postprandial fullness and early satiety within the preceding 3 months with symptom onset at least 6 months earlier [4]. Functional dyspepsia has a complex underlying pathophysiological mechanism that involves changes in gastric motility, visceral hypersensitivity, genetic susceptibility, psychosocial factors and *Helicobacter pylori* infection [5, 6].

Recent data supports the theory that *H. pylori* eradication provides significant benefits to patients with FD [7–11]. The Maastricht IV Consensus Report recommends this form of treatment [8]. Although there are several *H. pylori* eradication treatments, there is not enough data that compare these different eradication treatments for FD symptom resolution. Most previous studies have focused on the eradication rates of *H. pylori* rather than symptom relief in FD.

Aim

In this regard, we aimed to clarify if there is any difference between standard triple therapy and sequential therapy for symptom resolution of FD patients with *H. pylori* using a validated health quality index.

Material and methods

This study was a randomised single-blind clinical trial. The study was conducted in a single hospital, Ankara Research and Education Hospital, Ankara, Turkey. The local institutional review board approved the trial protocol. Written informed consent was obtained from all patients prior to enrolment. *Helicobacter pylori*–positive adult patients with functional dyspepsia meeting the Rome III International Consensus criteria were recruited. Endoscopy and rapid urease *H. pylori* tests were performed at screening. *Helicobacter pylori* positive patients were included into the study. A total of 194 patients were included in this study. Seventeen patients refused to participate in the study. The flowchart of patients throughout the study are shown in Figure 1. These patients were randomly assigned to receive standard triple therapy (omeprazole 20 mg twice daily, amoxicillin trihydrate 1000 mg twice daily and clarithromycin 500 mg twice daily for 14 days) or sequential therapy (omeprazole 20 mg twice daily plus amoxicilline 1000 mg twice daily for 7 days and omeprazole 20 mg twice daily, metronidazole 500 mg twice daily and clarithromycin 500 mg twice daily for a subsequent 7 days) by a "blinded" physician for H P. status (M.S). Outcome measures were based on symptomatic improvement at 12 months using a validated measure of subjective well-being (Gastrointestinal Symptom Rating Scale, GSRS). The GSRS is a disease-specific instrument, the development of which was based on reviews of gastrointestinal symptoms and clinical experience, to evaluate common symptoms of gastrointestinal disorders. The GSRS contains 15 items, each rated on a seven-point Likert scale from no discomfort to very severe discomfort. Based on a factor analysis, the 15 GSRS items break down into the following five scales: abdominal pain (abdominal pain, hunger pains and nausea); reflux syndrome (heartburn and acid regurgitation); diarrhoea syndrome (diarrhoea, loose stools and urgent need for defecation); indigestion syndrome (borborygmus, abdominal distension, eructation and increased flatus); and constipation syndrome (constipation, hard stools and feeling of incomplete evacuation). The scores are calculated by taking the mean of the items completed within an individual scale, with higher scores indicating greater severity of symptoms. The GSRS in European patient populations has a good internal consistency reliability and acceptable construct validity and responsiveness [12–14].

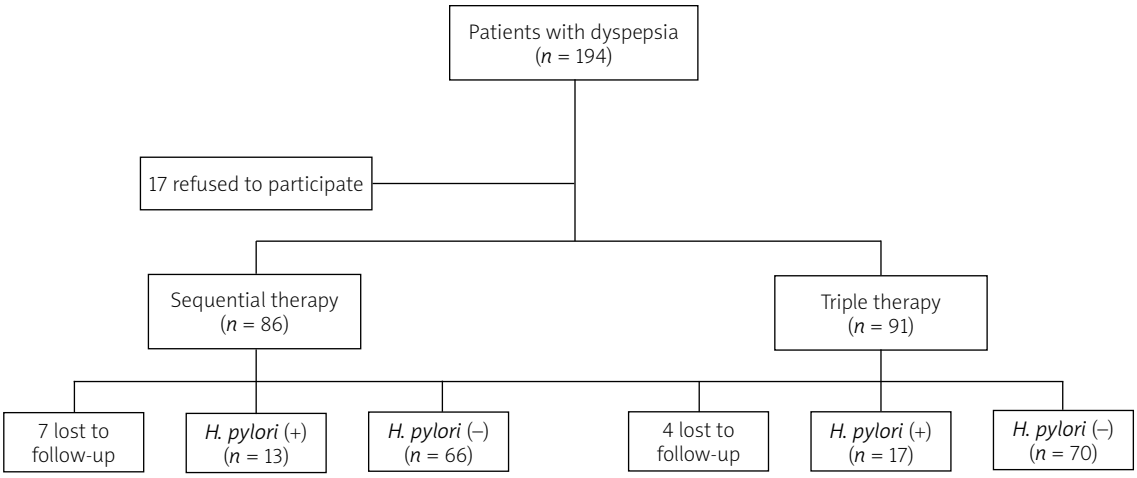

Figure 1. The flowchart of patients throughout the study

Table I. Demographic and clinical characteristics of the patients

Parameter	Sequential therapy (*n* = 66)	Triple therapy (*n* = 70)	Value of *p*
Age [years]	36.15 ±12.89	37.6 ±11.4	0.46
Male/female	25/41	24/46	0.66
GSRS scores (before treatment)	7.93 ±3.98	8.97 ±3.43	0.108
GSRS scores (after treatment)	3.54 ±2.98	3.92 ±2.94	0.45

Helicobacter pylori status was checked at 12 weeks with urea-breath test, and patients were excluded to eliminate the effect of persistent *H. pylori* on FD.

Patients of either sex were enrolled in the study if they were 18 years or older and had a diagnosis of *H. pylori* infection and functional dyspepsia according to the Rome III International Consensus criteria.

Exclusion criteria are as follows: predominant symptoms of heartburn or irritable bowel syndrome; alarm symptoms; history of peptic ulcer, upper gastrointestinal tract surgery, or biliary colic; previous treatment for eradication of *H. pylori*; known allergies to study medication; serious comorbidities; or alcohol or drug abuse. Use of antibiotics or bismuth during the 4 weeks before enrolment and proton pump inhibitors during the 2 weeks before enrolment were also among the exclusion criteria. Women of childbearing potential; patients unable to answer the study questionnaires; patients with endoscopic findings other than gastritis, duodenitis, or hiatal hernia; and patients unwilling or unable to provide consent were also excluded.

Statistical analysis

Statistical analyses were performed by SPSS statistical software (version 15.0 for Windows; SPSS Inc, Chicago, IL, U.S.A). All data were presented as the mean ± SD. Independent samples *t*-tests were used to compare groups. We evaluated within-group changes with paired samples *t*-test. Values of *p* less than 0.05 were considered statistically significant.

Results

Eradication rates of sequential and standard triple therapy were 83.54% and 80.4%, respectively. The gender and age of both treatment groups was quite similar (Table I). We observed a significant symptom resolution at 12 months in both treatment groups (Table II). On the other hand, there was no difference between the sequential or standard triple therapy groups regarding the alleviation of symptoms (Table I).

Table II. GSRS score changes in both groups

Therapy	Mean ± SD	Value of *p*
Sequential	4.39 ±3.16	< 0.001
Triple	5.04 ±2.91	< 0.001

Discussion

Many patients seek medical help for FD that cannot be explained easily. Furthermore, treatment of patients with non-ulcer dyspepsia can be challenging, mostly due to obscure pathogenesis on an individual basis. Possible pathophysiological mechanisms for non-ulcer dyspepsia include augmented visceral pain perception, bile reflux into the stomach, gastric motility, visceral hypersensitivity, genetic susceptibility, psychosocial factors, viral-induced gastritis, malabsorption of carbohydrates, parasitic infections and *H. pylori* infection. There is little objective evidence to support a major role for any of these factors, and purported involvement for many of them is based on case reports. Management of FD includes general measures, acid-suppressive drugs, pro-kinetic agents, fundus-relaxing drugs, antidepressants and psychological interventions [15, 16]. The most prevalent theory currently being considered is the possible involvement of *H. pylori* infection in FD (as in ulcer disease). That is why eradication of *H. pylori* is one of the most important topics for physicians concerning FD therapy.

In our study, *H. pylori* eradication yielded a good GSRS response in both treatment groups. We speculate that *H. pylori* plays a major role in FD pathogenesis in *H. pylori* positive patients with FD. Therefore, *H. pylori* should not be overlooked when considering the pathophysiology of FD, especially in countries with high *H. pylori* prevalence. Similarly, in a recent study from Singapore [9], the benefits of *H. pylori* eradication therapy among patients with FD is reported to give as much as a 13-fold increase in the chance of symptom resolution. The authors suggested that *H. pylori*-associated dyspepsia might be dealt with as a different disease entity from FD regarding this study. Although several *H. pylori* eradication therapies exist, there is no suggested *H. pylori* eradication therapy for FD. When a doctor decides to prescribe an eradication treatment, the presence of FD does not have a remarkable impact on antibiotic preferences. As everybody expects, eradication schemes are chosen mostly according to general rules such as bacterial resistance patterns and regional drug supply conditions, etc. In our study, we did not observe a significant difference between sequential or triple therapy for FD symptom resolution. We hereby speculate that the choice of eradication scheme has no effect, but only eradication it self is important in FD.

There are some limitations to our study. The first of which is the placebo effect of drug treatment. As shown in previous studies, the placebo effect cannot be ignored in the field of FD. The second limitation is the relatively small size of the study population. This is mostly due to limited patient compliance. We should hereby declare that it is not easy to recruit patients who accept a year-long study. Consequently, patient compliance in such patient groups in a study setting is a considerable problem [10].

Conclusions

Although management of dyspepsia or *H. pylori* eradication differs, eradication of *H. pylori* should be considered for a good clinical outcome in patients with FD in countries with high *H. pylori* prevalence. No difference for symptom relief exists between sequential and triple therapy in patients with FD. A better understanding of FD and its management can improve patient care and decrease unnecessary medical expenditures. Therefore, more studies are needed to resolve the effect of other *H. pylori* treatment regimens.

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