



## Double blind, randomised, placebo controlled study of four weeks of lansoprazole for the treatment of functional dyspepsia in Chinese patients

W M Wong, B C Y Wong, W K Hung, Y K Yee, A W C Yip, M L Szeto, F M Y Fung, T S M Tong, K C Lai, W H C Hu, M F Yuen and S K Lam

*Gut* 2002;51;502-506  
doi:10.1136/gut.51.4.502

---

Updated information and services can be found at:  
<http://gut.bmj.com/cgi/content/full/51/4/502>

---

*These include:*

### References

This article cites 18 articles, 1 of which can be accessed free at:  
<http://gut.bmj.com/cgi/content/full/51/4/502#BIBL>

1 online articles that cite this article can be accessed at:  
<http://gut.bmj.com/cgi/content/full/51/4/502#otherarticles>

### Email alerting service

Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article

---

### Topic collections

Articles on similar topics can be found in the following collections

[Randomized Controlled Trials: examples](#) (551 articles)  
[Other Epidemiology](#) (1675 articles)  
[Stomach and duodenum](#) (581 articles)  
[Drugs: gastrointestinal system](#) (502 articles)  
[Helicobacter Pylori](#) (396 articles)

---

### Notes

---

To order reprints of this article go to:  
<http://www.bmjournals.com/cgi/reprintform>

To subscribe to *Gut* go to:  
<http://www.bmjournals.com/subscriptions/>

## MOTILITY AND VISCERAL SENSATION

# Double blind, randomised, placebo controlled study of four weeks of lansoprazole for the treatment of functional dyspepsia in Chinese patients

W M Wong, B C Y Wong, W K Hung, Y K Yee, A W C Yip, M L Szeto, F M Y Fung, T S M Tong, K C Lai, W H C Hu, M F Yuen, S K Lam

*Gut* 2002;**51**:502–506

See end of article for authors' affiliations

Correspondence to:  
Dr B C Y Wong,  
Department of Medicine,  
University of Hong Kong,  
Queen Mary Hospital,  
Hong Kong;  
[bcywong@hku.hk](mailto:bcywong@hku.hk)

Accepted for publication  
28 January 2002

**Background:** The use of proton pump inhibitors for the treatment of functional dyspepsia is controversial and the role of *Helicobacter pylori* infection in functional dyspepsia is uncertain.

**Aim:** To evaluate the efficacy of different doses of lansoprazole for the treatment of functional dyspepsia in Chinese patients.

**Method:** Patients with a clinical diagnosis of functional dyspepsia according to the Rome II criteria and normal upper gastrointestinal endoscopy were recruited and randomised to receive: (1) lansoprazole 30 mg, (2) lansoprazole 15 mg, or (3) placebo, all given daily for four weeks. Dyspepsia symptom scores and quality of life (SF-36 score) were evaluated before and four weeks after treatment.

**Results:** A total of 453 patients were randomised. There was no difference in the proportion of patients with complete symptom relief in the lansoprazole 30 mg (23%) and lansoprazole 15 mg (23%) groups compared with the placebo group (30%). The proportion of *H pylori* positive patients with a complete response was similar with lansoprazole 30 mg (34%) and lansoprazole 15 mg (20%) versus placebo (22%). All symptom subgroups (ulcer-like, dysmotility-like, reflux-like, and unspecified dyspepsia) had similar proportions of patients with complete symptom relief after treatment.

**Conclusion:** Proton pump inhibitor treatment is not superior to placebo for the management of functional dyspepsia in Chinese patients.

According to the Rome II criteria, functional dyspepsia is defined as persistent or recurrent pain or discomfort centred in the upper abdomen for at least 12 weeks in the preceding 12 months.<sup>1</sup> In the Asia Pacific region, dyspepsia is as common as in the rest of the world, with a prevalence varying from 10% to 20%.<sup>2–5</sup> Functional dyspepsia or non-ulcer dyspepsia is a common problem encountered in gastroenterology. It is a significant cause of morbidity and time lost from work.<sup>6</sup> There is no definitive treatment for this condition. However, acid suppressive therapy such as H<sub>2</sub> antagonists or proton pump inhibitors is commonly used for the treatment of functional dyspepsia. There is some evidence that antisecretory therapy may be effective in non-ulcer dyspepsia, according to a meta-analysis.<sup>7</sup> On average, H<sub>2</sub> blockers have been shown to produce a 20% improvement in dyspepsia symptoms compared with placebo.<sup>8,9</sup> Recently, two large randomised controlled trials have been published to assess the efficacy of proton pump inhibitors for functional dyspepsia.<sup>10,11</sup> The earlier trial in which patients were treated with omeprazole 20 mg a day for four weeks showed a 10% gain over placebo but there was no relationship with *Helicobacter pylori* status.<sup>10</sup> A higher proportion of patients with ulcer-like and reflux-like dyspepsia had complete symptomatic relief with omeprazole 20 mg versus placebo but such benefit was not observed in patients with dysmotility-like dyspepsia. The second trial showed that a higher proportion of *H pylori* positive patients went into remission using omeprazole 20 mg a day for two weeks compared with placebo. But no significant benefit was observed in *H pylori* negative patients.<sup>11</sup> Another randomised controlled trial published in abstract form compared omeprazole 20 mg and placebo for the treatment of functional dyspepsia and found a higher complete response rate in the omeprazole group.<sup>12</sup> There are other trials in uninvestigated dyspepsia in the primary care setting but they are limited by lack of blinding,<sup>13</sup> absence of a

placebo group,<sup>14</sup> or selection of dyspepsia subgroups.<sup>15</sup> While the previous randomised placebo controlled trials were done in Western population, and with controversial results, we performed a double blind placebo controlled study to assess the efficacy of lansoprazole 30 mg and lansoprazole 15 mg versus placebo in Chinese patients. The therapeutic benefit in *H pylori* positive and *H pylori* negative patients was also assessed. Dyspepsia subgroups based on the predominant symptoms of the patients were studied to identify potential responders to acid suppressive therapy.

## METHODS

### Patient population

Consecutive patients referred to the endoscopy unit of the Department of Medicine, Queen Mary Hospital, Department of Medicine, Tuen Mun Hospital, and Department of Surgery, Kwong Wah Hospital, with a clinical diagnosis of functional dyspepsia and normal gastrointestinal endoscopy were assessed for recruitment. Functional dyspepsia was defined as persistent or recurrent dyspepsia (pain or discomfort centred in the upper abdomen) with no evidence of organic disease, chronic severe constipation, or irritable bowel syndrome to explain the symptoms, for at least 12 weeks, which need not be consecutive, within the preceding 12 months, in accordance with the Rome II criteria. Patient aged 18–80 years with symptoms of dyspepsia within two weeks prior to the endoscopy visit were eligible for the study. Informed written consent was obtained from all patients. Patients were also required to have a dyspepsia score of greater than 16 by our validated questionnaire<sup>16</sup> and had no prior investigations performed for this episode of dyspepsia

**Abbreviations:** ITT, intention to treat; PP, per protocol.

within six months before the study. Exclusion criteria included patients who had any erosive change in the oesophagus, stomach, or duodenum, oesophageal stricture, Barrett's oesophagus, duodenal deformity, or gastric or duodenal ulcer; past history of peptic ulcer disease by endoscopy or radiology; past history of gastro-oesophageal reflux disease documented by upper endoscopy or 24 hour oesophageal pH monitoring; severe concomitant illness; pregnancy or lactation; alcohol or drug abuse; and use of aspirin or other non-steroidal anti-inflammatory drugs, antibiotics, H<sub>2</sub> receptor blockers, bismuth, or proton pump inhibitors in the preceding four weeks. Patients with classical heartburn or acid regurgitation as their only symptom without epigastric discomfort or pain were also excluded to avoid recruitment of patients with undiagnosed gastro-oesophageal reflux disease. The study was approved by the local ethics committees in the various hospitals.

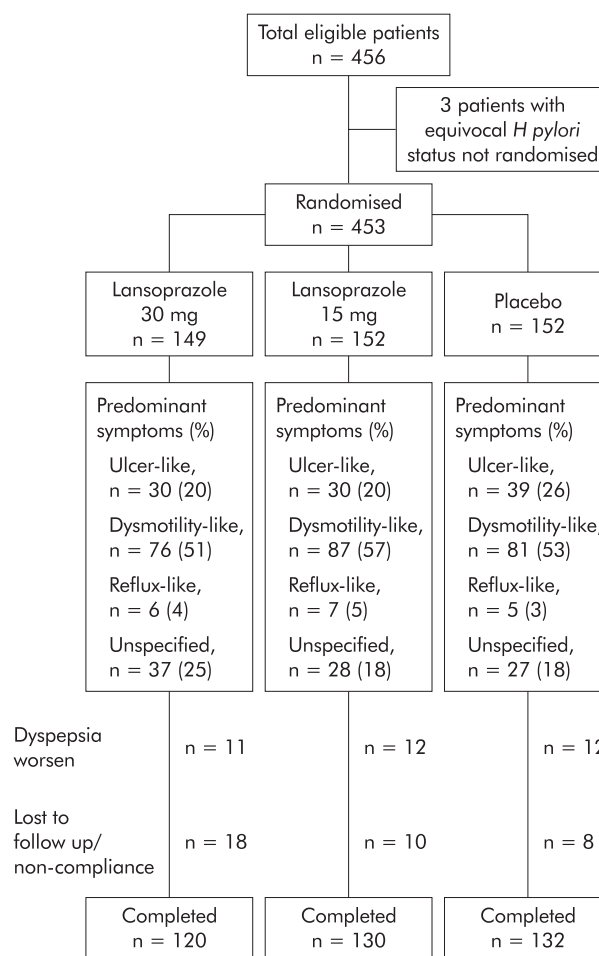
### Diagnosis of *H pylori* infection

During endoscopy, two antral biopsies and one corpus biopsy were obtained. One antral biopsy was used for a locally validated rapid urease test.<sup>17</sup> The other biopsies were sent for histological examination of *H pylori* status by haematoxylin-eosin stains and Giemsa stain if necessary. Specimens were read by experienced pathologists who were blinded to all clinical information, including the rapid urease test results. The definition of *H pylori* infection in this study required both tests to be positive. Equivocal cases were excluded from the study. This approach has been previously validated in our centre, with an accuracy of 100%, and less than 0.3% of cases cannot be diagnosed by this approach.<sup>17</sup> Both patients and the managing physicians were blinded to *H pylori* status.

### Treatment regimen

Patients were randomised to receive one of the following treatments: (1) 30 mg of lansoprazole; (2) 15 mg of lansoprazole, or (3) placebo, all given once daily for four weeks. Randomisation was performed by drawing a sealed envelope that contained a pre-assigned randomised treatment generated by computer on entry to the study. Both the investigators and patients were blinded to the assigned treatment throughout the study. The lansoprazole and placebo capsules were identical in appearance. Patients were given a diary in which they recorded side effects and symptoms during therapy. Patients returned for follow up four weeks later and gastroenterologists assessed their symptoms and quality of life. Patient compliance was checked by counting returned study medications. Patients were not allowed to take antacids, H<sub>2</sub> receptor blockers, bismuth, antibiotics, or proton pump inhibitors during the study period.

Dyspepsia symptoms were assessed by a locally validated dyspepsia questionnaire which consisted of 12 questions (epigastric pain, upper abdominal bloating, upper abdominal dull ache, epigastric pain before meals, epigastric pain when anxious, vomiting, nausea, belching, acid regurgitation, heartburn, feeling of acidity in the stomach, loss of appetite) and graded on a five point Likert scale as follows: 1 (none), no symptoms; 2 (mild), symptoms can be easily ignored; 3 (moderate), awareness of symptoms but easily tolerated; 4 (severe), symptoms sufficient to cause interference with normal activities; 5 (incapacitating), incapacitating symptoms with an inability to perform daily activities and/or require days off work. Test-retest reproducibility and internal consistency were good, with an intraclass correlation coefficient of 0.89 and Cronbach's alpha coefficient of 0.90. A cut off score of  $\geq 16$  was discriminative between controls and dyspeptic patients, as well as those who reported a subjective improvement in symptoms and those who reported no change or worsening after treatment.<sup>16</sup> Patients were then subclassified into four dyspepsia subgroups according to their predominant symptoms: (1) ulcer-like dyspepsia—predominant epigastric pain; (2) dysmotility-like dyspepsia—predominant discomfort that



**Figure 1** Flow chart of the study patients.

may be characterised by upper abdominal fullness, early satiety, bloating, or nausea; (3) reflux-like dyspepsia—predominant reflux symptoms (heartburn or acid regurgitation); (4) unspecified—symptoms do not fulfill the criteria for ulcer-like, dysmotility-like, or reflux-like dyspepsia. Although reflux-like dyspepsia was discarded in the Rome II criteria, we felt that a certain proportion of patients with functional dyspepsia still belong to that particular subgroup and there is considerable overlap between functional dyspepsia and non-erosive or negative endoscopy reflux disease.<sup>18,19</sup> Furthermore, inclusion of reflux-like dyspepsia allows comparison with previous randomised controlled trials.<sup>10</sup> Quality of life was assessed by a locally validated questionnaire (Chinese translated form of SF-36).<sup>20</sup> The SF-36 consisted of 11 items to measure eight aspects of psychological general well being (physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health).

### Statistical analysis

Treatment success was defined as complete relief of epigastric pain/discomfort (that is, no symptoms) during the last three days of the four week treatment. The proportion of patients with complete relief of epigastric pain/discomfort was compared between the lansoprazole 30 mg and 15 mg groups and the placebo group. Mean dyspepsia score and the eight aspects of the SF-36 scores before and after treatment were compared in the three treatment groups. The change in mean dyspepsia score and SF-36 scores from baseline to the four week visit were calculated and compared between the lansoprazole 30 mg and 15 mg groups and the placebo group.

**Table 1** Demographics of the patient population

	Lansoprazole 30 mg	Lansoprazole 15 mg	Placebo
No of patients (intention to treat)	149	152	152
Age (y) (mean (SD))	42.7 (12.1)	42.9 (13.5)	41.6 (13.5)
Sex (M/F)	44/105	38/114	36/116
Smokers (%)	14	11	11
Previous smoker (%)	3	3	3
Alcohol (%)	4	5	4
Duration of disease >1 y (%)	79	80	78
<i>H pylori</i> positive (%)	59 (40)	55 (36)	59 (39)
Predominant symptoms (%)			
Ulcer-like	30 (20)	30 (20)	39 (26)
Dysmotility-like	76 (51)	87 (57)	81 (53)
Reflux-like	6 (4)	7 (5)	5 (3)
Unspecified	37 (25)	28 (18)	27 (18)

**Table 2** Complete relief of dyspeptic symptoms, respective *Helicobacter pylori* status, and dyspepsia subtypes of the three treatment groups

	Lansoprazole 30 mg	Lansoprazole 15 mg	Placebo
Complete relief of symptoms			
Intention to treat	23% (35/149)	23% (35/152)	30% (45/152)
(95% CI)	(17–31)	(17–30)	(23–37)
Per protocol	29% (35/120)	27% (35/130)	34% (45/132)
(95% CI)	(21–38)	(20–35)	(26–43)
Complete relief of symptoms			
<i>H pylori</i> positive	34% (20/59)	20% (11/55)	22% (13/59)
<i>H pylori</i> negative	16% (15/90)	25% (24/97)	34% (32/93)
Complete relief of symptoms			
Ulcer-like	30% (9/30)	30% (9/30)	26% (10/39)
Dysmotility-like	21% (16/76)	20% (17/87)	28% (23/81)
Reflux-like	17% (1/6)	0% (0/7)	20% (2/5)
Unspecified	24% (9/37)	32% (9/28)	37% (10/27)

### Power of the study

An expected placebo complete response rate of 25% was adopted. To detect a 20% difference in the efficacy of the two treatment regimens versus placebo with a power of 80% and an  $\alpha$  error of 5%, at least 98 patients in each arm were required. Assuming 20% of patients would dropout, at least 123 patients were required in each treatment group.

A  $\chi^2$  test, Fisher's exact test, and the Student's *t* test were used; the Mann-Whitney U (non-parametric) test was used for data with a skewed distribution. A *p* value of 0.05 or less was considered statistically significant. The intention to treat (ITT) analysis included all patients who had taken at least one tablet. In the per protocol (PP) analysis, patients with poor drug compliance (<75% intake of any study drugs) and dropouts (due to adverse effects) were excluded. Multiple logistic regression analysis was performed to determine the factors (age, sex, *H pylori* status, smoking, alcohol intake, dyspepsia duration, predominant symptoms, and type of treatment given) associated with a complete response.

### RESULTS

We recruited 456 eligible patients. Of these, 129 (28%) were referred for an open access endoscopy by primary care physicians and the remainder were referred by gastroenterologists. Three had an equivocal *H pylori* status, leaving 453 patients for the ITT analysis (fig 1). A total of 149 patients were randomised to receive lansoprazole 30 mg, 152 patients were randomised to receive lansoprazole 15 mg, and 152 patients were randomised to receive placebo. All recruited patients were ethnic Chinese. Baseline characteristics of the patients in the three treatment groups are given in table 1. Compliance was satisfactory and more than 81%, 86%, and 87% of patients

took more than 75% of the medications in the lansoprazole 30 mg, lansoprazole 15 mg, and placebo groups, respectively. Poor compliance patients, those who refused follow up, and those who discontinued treatment because of adverse events were excluded from the PP analysis (n=382) (fig 1). Baseline characteristics of the patients and their dyspepsia subtypes are listed in table 1. Mean age of these patients was 42.4 (range 18–75) years with a median dyspepsia score of 21.0. There were 118 males (mean age 45.3 years) and 335 females (mean age 41.4 years). Mean age, sex distribution, smoking history, alcohol consumption, proportion of patients with dyspepsia for more than one year, *H pylori* positivity, and mean dyspepsia score at baseline were similar between the three treatment groups (tables 1, 3).

There was no difference in the proportions of patients with complete symptom relief in the lansoprazole 30 mg (ITT=23%, PP=29%) and lansoprazole 15 mg (ITT=23%, PP=27%) groups versus placebo (ITT=30%, PP=34%) (table 2). When complete symptom relief was assessed according to symptom subtypes, there was no difference between lansoprazole 30 mg and lansoprazole 15 mg versus placebo for all symptom subgroups (table 2). The presence or absence of heartburn did not predict a complete response to lansoprazole 30 mg or lansoprazole 15 mg versus placebo (NS).

### *Helicobacter pylori* (table 2)

A total of 173 patients (38%) were *H pylori* positive by our gold standard. The proportion of *H pylori* positive patients with complete response was similar in the lansoprazole 30 mg (34%) and lansoprazole 15 mg (20%) groups compared with placebo (22%) (NS). In *H pylori* negative patients, a complete response rate was higher in the placebo group compared with the lansoprazole 30 mg group (34% v 16%; *p*=0.01).

**Table 3** Mean dyspepsia score and SF-36 (mean (SEM)) at week 0 and week 4 in the three treatment groups

	Week 0	Week 4	p Value
Mean dyspepsia score			
Lansoprazole 30 mg	21.7 (0.3)	18.6 (0.4)	<0.001
Lansoprazole 15 mg	22.3 (0.4)	19.0 (0.4)	<0.001
Placebo	22.1 (0.4)	18.7 (0.5)	<0.001
SF36-physical functioning			
Lansoprazole 30 mg	87.6 (1.1)	87.0 (1.2)	NS
Lansoprazole 15 mg	88.7 (1.2)	85.6 (1.4)	0.029
Placebo	88.6 (1.1)	88.0 (1.2)	NS
SF36-role physical			
Lansoprazole 30 mg	58.7 (3.2)	71.8 (6.1)	0.027
Lansoprazole 15 mg	60.7 (2.9)	61.5 (3.1)	NS
Placebo	66.2 (3.0)	75.3 (2.6)	0.007
SF36-bodily pain			
Lansoprazole 30 mg	55.2 (1.6)	65.8 (1.6)	<0.001
Lansoprazole 15 mg	56.1 (1.7)	64.4 (1.7)	<0.001
Placebo	56.6 (1.6)	66.2 (1.8)	<0.001
SF36-general health			
Lansoprazole 30 mg	46.5 (1.4)	46.7 (1.5)	NS
Lansoprazole 15 mg	45.1 (1.3)	44.6 (1.4)	NS
Placebo	45.5 (1.4)	45.7 (1.6)	NS
SF36-vitality			
Lansoprazole 30 mg	53.0 (1.5)	57.8 (1.5)	0.004
Lansoprazole 15 mg	51.4 (1.5)	53.6 (1.7)	NS
Placebo	53.7 (1.4)	54.7 (1.5)	NS
SF36-social function			
Lansoprazole 30 mg	55.2 (1.6)	65.8 (1.6)	NS
Lansoprazole 15 mg	56.1 (1.7)	64.4 (1.7)	NS
Placebo	56.6 (1.6)	66.2 (1.8)	NS
SF36-role emotional			
Lansoprazole 30 mg	55.7 (3.5)	62.9 (3.4)	0.039
Lansoprazole 15 mg	55.5 (3.1)	60.5 (3.3)	NS
Placebo	59.6 (3.3)	71.7 (3.1)	0.001
SF36-mental health			
Lansoprazole 30 mg	64.5 (1.2)	66.5 (1.2)	NS
Lansoprazole 15 mg	61.8 (1.3)	63.6 (1.4)	NS
Placebo	61.7 (1.4)	64.9 (1.3)	0.018

### Mean dyspepsia score and quality of life assessment (table 3)

Baseline dyspepsia scores and quality of life assessments were similar in the three treatment groups. Mean dyspepsia score improved in all three groups at week 4 compared with baseline. Four parameters of quality of life assessment (role physical, bodily pain, vitality, and role emotional) improved significantly at week 4 compared with baseline in the lansoprazole 30 mg group. Two parameters of quality of life assessment (physical functioning and bodily pain) improved significantly at week 4 compared with baseline in the lansoprazole 15 mg group. In the placebo group, four parameters of quality of life assessment (role physical, bodily pain, role emotional, and mental health) improved significantly at week 4 compared with baseline. However, the change in mean dyspepsia score and SF-36 score from baseline to the four week visit were similar between lansoprazole 30 mg versus placebo and lansoprazole 15 mg versus placebo (NS, data not shown). Subjects were divided into those with dyspepsia scores above and below the median score of 21.0. There were no significant differences in complete symptom relief among the two lansoprazole groups and the placebo group in both subjects with moderate to severe dyspepsia (dyspepsia score  $\geq 21.0$ ) and subjects with mild dyspepsia (dyspepsia score  $< 21.0$ ).

### Adverse events (fig 1)

A total of 35 patients (11 on lansoprazole 30 mg, 12 on lansoprazole 15 mg, and 12 on placebo) discontinued treatment due to adverse effects. In general, medications were well tolerated in all three groups.

### Factors associated with complete response

Age, sex, *H pylori* status, smoking, alcohol consumption, and dyspepsia duration had no effect on the complete response rate. Using multiple logistic regression analysis, which included the predominant symptoms and type of treatment given in addition to the above factors, we could not identify any particular factor that was associated with a favourable outcome.

### DISCUSSION

We have reported a double blind, randomised, placebo controlled study of lansoprazole 30 mg and 15 mg versus placebo for the treatment of functional dyspepsia. We found that there was no difference in the proportions of patients with complete symptom relief between the lansoprazole 30 mg (23%) and 15 mg (23%) groups versus the placebo group (30%). All symptom subgroups had similar proportions of patients with complete symptom relief after treatment. The proportion of *H pylori* positive patients with a complete response was similar in the lansoprazole 30 mg (34%) and 15 mg (20%) groups versus the placebo group (22%). However, a higher placebo response rate was observed in the *H pylori* negative group.

In contrast with the Bond and Opera studies,<sup>10</sup> we failed to demonstrate the beneficial effect of proton pump inhibitor versus placebo for the treatment of functional dyspepsia. The Bond and Opera studies reported their results in a combined fashion, which consisted of two identically designed randomised controlled trials. However, when the two trials were analysed separately, the observed benefits were only found in the former study. The authors attributed the observed difference to a higher proportion of patients being recruited

from family practice in the Bond study compared with the Opera study, which had a higher placebo response rate among patients seeing a gastroenterologist. A relatively high placebo response rate (30%) was observed in our patients who were attended by gastroenterologists during the initial treatment and subsequent follow up. Thus the argument proposed by Talley *et al*, where patients seeing a specialist may feel more assured after a normal upper endoscopy leading to a higher placebo response, also applied to our patients.<sup>10</sup>

In contrast with our study, the definition of primary outcome in the study of Blum *et al* was disappearance of dyspeptic symptoms requiring further management after a two week course of omeprazole 20 mg daily, omeprazole 10 mg daily, ranitidine 150 mg daily, or placebo.<sup>11</sup> A significant therapeutic benefit was observed only in *H pylori* positive patients in the omeprazole 20 mg group. However, the investigators were not blinded to the *H pylori* status of the patients, which may preclude the validity of their results. *H pylori* positive patients not responding to treatment were allowed to enter into a second study to examine the effect of *H pylori* eradication on functional dyspepsia. As pointed out by McColl,<sup>21</sup> the lower therapeutic response observed in *H pylori* positive patients in all treatment groups compared with *H pylori* negative patients suggested that the investigators were much less inclined to recognise a beneficial response in *H pylori* infected patients. The proportion of patients showing a therapeutic response following omeprazole treatment was greater in *H pylori* negative patients (71%) compared with *H pylori* positive patients (59%), despite the effectiveness of omeprazole over placebo being confined to the latter group. Thus the much lower placebo response rate in the *H pylori* positive patients may have contributed to the benefit of omeprazole versus placebo being observed only in the *H pylori* positive group. Both the managing physicians and patients were blinded to the *H pylori* data in our study. In contrast, we did not observe a therapeutic benefit of lansoprazole 30 mg or lansoprazole 15 mg versus placebo. The fact that a significantly higher placebo response rate was observed in *H pylori* negative patients is probably a chance finding.

Classification of dyspepsia patients into symptom subgroups did not identify a particular subgroup that responded better to lansoprazole treatment. It has been suggested that atypical gastro-oesophageal reflux disease may explain the benefit of acid suppression observed in trials of functional dyspepsia.<sup>22-24</sup> It should be noted that only approximately 4% of the patients in our study reported acid reflux symptoms as their predominant symptoms and the majority of patients had dysmotility-like symptoms (54%) as their predominant symptoms. Furthermore, the presence or absence of heartburn did not predict a complete response to lansoprazole versus placebo. Thus the contribution of atypical gastro-oesophageal reflux disease to a better response to lansoprazole appeared to be small in our study.

Patients with various degree of dyspepsia were enrolled according to the inclusion criteria, ranging from a score of 17 (mild) and above. Judging from the median dyspepsia score of 21.0, 50% of patients had a dyspepsia score of greater than 21.0, indicating that at least half had moderate to severe dyspepsia. Further analysis failed to show the superiority of lansoprazole over placebo in both the severe dyspepsia group (those with a score  $\geq 21.0$ ) and the mild dyspepsia group (those with a score  $< 21.0$ ).

In conclusion, our data suggest that a proton pump inhibitor was not superior to placebo for the management of functional dyspepsia in Chinese patients.

#### ACKNOWLEDGEMENTS

The authors would like to thank Drs CK Chan, G Lau, CK Hui, and OO Chan of Queen Mary Hospital; Drs KF Li, CK Lee, KF Chang, Grace SW Wong, and SF Lau of Department of Medicine, Tuen Mun Hospital; Drs P Lau, Maket WC Wong, J Hui, and TW Chow of Department of Surgery, Kwong Wah Hospital for performing some of the endoscopies;

YH Wong for some of the data management; and the endoscopy nurses of the three participating centres for nursing assistance. This study was supported by an unrestricted grant from Takeda Chemical Industries (Taiwan) Ltd, Simon KY Lee Gastroenterology Research Fund, and Peptic Ulcer Research Fund, University of Hong Kong.

#### Authors' affiliations

**W M Wong†, B C Y Wong†, F M Y Fung, T S M Tong, K C Lai, W H C Hu, M F Yuen, S K Lam**, Department of Medicine, University of Hong Kong, Queen Mary Hospital, Hong Kong  
**W K Hung, A W C Yip**, Department of Surgery, Kwong Wah Hospital, Hong Kong  
**Y K Yee, M L Szeto**, Department of Medicine, Tuen Mun Hospital, Hong Kong

†W M Wong and B C Y Wong contributed equally to this work.

#### REFERENCES

- Talley NJ, Stanghellini V, Heading RC, *et al*. Functional gastroduodenal disorders. *Gut* 1999;**45**(suppl II):37-42.
- Lam SK, Talley NJ. Report of the 1997 Asia Pacific Consensus Conference on the management of *Helicobacter pylori* infection. *J Gastroenterol Hepatol* 1998;**13**:1-12.
- Talley NJ, Lam SK, Goh KL, *et al*. Management guidelines for uninvestigated and functional dyspepsia in the Asia-Pacific region: First Asian Pacific Working Party on Functional Dyspepsia. *J Gastroenterol Hepatol* 1998;**13**:335-53.
- Hu WHC, Hui WM, Lam SK. Anxiety and depression are co-factors determining health care utilization in patient with dyspepsia: A Hong Kong population based study. *Gastroenterology* 1997;**112**:A153.
- Ho KY, Kang JY, Seow A. Prevalence of gastrointestinal symptoms in a multiracial Asian population, with particular reference to reflux-type symptoms. *Am J Gastroenterol* 1998;**93**:1816-22.
- Nyrén O, Adami HO, Gustavsson S, *et al*. Social and economic effects of non-ulcer dyspepsia. *Scand J Gastroenterol* 1985;**109**(suppl):41-7.
- Soo S, Maayyedi P, Deeks J, *et al*. Pharmacological interventions for non-ulcer dyspepsia. *Cochrane Database Syst Rev* 2000;**2**:CD001960.
- Finney JS, Kinnersley N, Hughes M, *et al*. Meta-analysis of antisecretory and gastrokinetic compounds in functional dyspepsia. *J Clin Gastroenterol* 1998;**26**:312-20.
- Dobrilla G, Comberlato M, Steele A, *et al*. Drug treatment of functional dyspepsia: a meta-analysis of randomized controlled clinical trials. *J Clin Gastroenterol* 1989;**11**:169-77.
- Talley NJ, Meineche-Schmidt V, Paré P, *et al*. Efficacy of omeprazole in functional dyspepsia: double-blind randomized placebo-controlled trials (the Bond and Opera studies) *Aliment Pharmacol Ther* 1998;**12**:1055-65.
- Blum AL, Arnold R, Stolte M, *et al*. Short course acid suppressive treatment for patients with functional dyspepsia: results depend on *Helicobacter pylori* status. *Gut* 2000;**47**:473-80.
- Lauritsen K, Aalykke C, Havelund T, *et al*. Effect of omeprazole in functional dyspepsia: A double-blind, randomized, placebo-controlled study. *Gastroenterology* 1996;**4**:A702.
- Goves J, Oldring JK, Kerr D, *et al*. First line treatment with omeprazole provides an effective and superior alternative strategy in the management of dyspepsia compared to antacid/alginate liquid: a multicentre study in general practice. *Aliment Pharmacol Ther* 1998;**12**:147-57.
- Jones RH, Baxter G. Lansoprazole 30 mg daily versus ranitidine 150mg b.d. in the treatment of acid-related dyspepsia in general practice. *Aliment Pharmacol Ther* 1997;**11**:541-6.
- Meineche-Schmidt V, Krag E. Antisecretory therapy in 1017 patients with ulcerlike or refluxlike dyspepsia in general practice. *Eur J Gen Pract* 1997;**3**:125-30.
- Hu WHC, Lam KF, Wong YH, *et al*. The Hong Kong index of dyspepsia: A validated symptom severity questionnaire for patients with dyspepsia. *J Gastroenterol Hepatol* 2002;**17**:545-51.
- Wong BCY, Wong WM, Wang WH, *et al*. An evaluation of invasive and non-invasive tests for the diagnosis of *Helicobacter pylori* infection in Chinese—the best tests for routine clinical use and research purpose. *Aliment Pharmacol Ther* 2001;**15**:505-11.
- Quigley EM. Non-erosive reflux disease: part of the spectrum of gastro-oesophageal reflux disease, a component of functional dyspepsia, or both? *Eur J Gastroenterol Hepatol* 2001;**13**(suppl 1):S13-8.
- Delaney BC, Innes MA, Deeks J, *et al*. Initial management strategies for dyspepsia. *Cochrane Database Syst Rev* 2001;**3**:CD001961.
- Lam CL, Gandek B, Ren XS, *et al*. Tests of scaling assumptions and construct validity of the Chinese (HK) version of the SF-36 Health Survey. *J Clin Epidemiol* 1998;**51**:1139-47.
- McColl KEL. No *H. pylori*: less dyspepsia? *Gut* 2000;**47**:461-2.
- Farup PG, Hovde O, Breder O. Are frequent short gastroesophageal reflux episodes the cause of symptoms in patients with non-ulcer dyspepsia responding to treatment with ranitidine? *Scand J Gastroenterol* 1995;**30**:829-32.
- Small PK, Loudon MA, Waldron B, *et al*. Importance of reflux symptoms in functional dyspepsia. *Gut* 1995;**36**:189-92.
- Farup PG, Hovde O, Torp R, *et al*. Patients with functional dyspepsia responding to omeprazole have a characteristic gastro-oesophageal reflux pattern. *Scand J Gastroenterol* 1999;**34**:575-9.