A Randomized, Double-Blind, Multicenter, Placebo-Controlled Trial of Qi-Zhi-Wei-Tong Granules on Postprandial Distress Syndrome-Predominant Functional Dyspepsia

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Abstract

Background: Functional dyspepsia (FD) is a common upper gastrointestinal disorder worldwide, but the current treatments for FD are still unsatisfactory. The aims of this study were to investigate the efficacy and safety of Qi-Zhi-Wei-Tong granules in patients with postprandial distress syndrome (PDS)-predominant FD.

Methods: The study was conducted as a randomized, double-blinded, multicenter, placebo-controlled design in 197 patients with PDS. All participants received placebo treatment for 1 week. Patients whose total symptom score decreased by <50% after the placebo treatment were recruited into the 4-week treatment period, in which they were randomly assigned to be treated with either Qi-Zhi-Wei-Tong granules or placebo. The patients were then followed for 2 weeks without any treatment. Dyspeptic symptoms were scored at weeks 2 and 4 during the random treatment period and 2 weeks after the treatment. Anxiety and depression symptoms were also scored and compared.

Results: (1) The total effective rates in the Qi-Zhi-Wei-Tong granules group at weeks 2 and 4 during the random treatment period and 2 weeks after treatment were all significantly higher than those in the placebo group (38.82% vs. 8.75%, $P < 0.001$; 69.14% vs. 16.25%, $P < 0.001$; 77.65% vs. 21.25%, $P < 0.001$). (2) The total dyspeptic symptoms scores in the Qi-Zhi-Wei-Tong granules group at weeks 2 and 4 and 2 weeks after treatment were significantly lower than those in the placebo group. (3) The severity and frequency of each dyspeptic symptom at weeks 2 and 4 and the follow-up period were all significantly lower than those in the placebo group. (4) The anxiety scores in the Qi-Zhi-Wei-Tong granules group were significantly lower than those in the placebo group. (5) Qi-Zhi-Wei-Tong granules did not have more adverse effects than the placebo.

Conclusion: Qi-Zhi-Wei-Tong granules offer significant symptomatic improvement in PDS with no more adverse effects than placebo.

Trial Registration: https://clinicaltrials.gov/, NCT02460601.

Key words: Clinical Trial; Functional Dyspepsia; Postprandial Distress Syndrome; Qi-Zhi-Wei-Tong Granules

Introduction

Functional dyspepsia (FD) is a common upper gastrointestinal disorder that occurs in 11–29% of the population globally.[1] Patients with FD usually complain of chronic or recurrent epigastric pain, epigastric burning, postprandial fullness, and early satiety, which severely impair patients' quality of life.[2] In general, FD is divided into two subtypes according to the

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main complaints: epigastric pain syndrome, in which the patients mainly complain of epigastric pain and/or burning, and postprandial distress syndrome (PDS), in which the patients mainly complain of postprandial fullness and/or early satiety.[3] It is believed that disturbed gastrointestinal functions, including gastrointestinal motility dysfunction, visceral sensitivity disorder, *Helicobacter pylori* infection, and psychosocial problems, are the main causes of the disorder since no identifiable structural lesions can be found in the clinical setting.[4]

The current treatments for FD are still unsatisfactory. In clinical practice, for patients with PDS, prokinetics, such as domperidone, cisapride, erythromycin, and metoclopramide, are the mainly used. However, the effects are limited and the cardiac side effects restrict their clinical use.[5] Therefore, finding a safe and convincingly effective drug is essential to the treatment of this disease.

Qi-Zhi-Wei-Tong granules are a commercially available preparation used for the treatment of the dyspepsia symptoms and are composed of six types of Chinese herbals: *Radix Bupleuri, Corydalis Rhizoma, Fructus Aurantii, Nutgrass Galingale Rhizome, White Peony Root, and Glycyrrhizae Radix Et Rhizoma Praeparata Cum Melle*. Previous small-size open-label studies in China have shown the beneficial effect of Qi-Zhi-Wei-Tong granules on the treatment of FD.[6,7] Nevertheless, these short-term, open-label studies cannot well exclude the placebo effect or the spontaneous fluctuation of symptoms. Side effects of the medicine were also rarely observed. Therefore, we designed the randomized, placebo-controlled, multicenter trial to assess the efficacy and safety of Qi-Zhi-Wei-Tong granules for PDS.

Methods

Ethic approval

The study protocol (https://clinicaltrials.gov/, NCT02460601) was approved by the Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology, and all the other institutions. The study was performed in accordance with the *Declaration of Helsinki* and *Good Clinical Practice for Trials on Pharmaceutical Products* by the China Food and Drug Administration. Written informed consent was signed before enrollment and patients were free to withdraw from the trial at any time.

Patients and methods

A total of 197 patients, aged between 18 and 65 years, with PDS symptoms who met the diagnostic criteria for functional gastrointestinal disease outlined in Rome III[8] were recruited by investigators from nine tertiary referral centers in China from February 2013 to April 2015. All patients had experienced symptoms of chronic or intermittent postprandial fullness or early satiety for over 3 of the previous 6 months. Before enrollment in the trial, a physical examination, laboratory test (including full blood count, fasting blood glucose, liver function, and renal function), upper abdominal ultrasound, and gastroscopy were performed to exclude structural diseases that might cause dyspepsia symptoms. In addition, to improve the evaluation of the results, symptom scores were defined as ≥4 on a 5-point adjectival scale linked to the effect exerted by symptoms on usual activities. Patients whose concomitant was medication acting on or influencing the gastrointestinal system (such as proton-pump inhibitors, H2 blockers, cholagogues, prokinetic agents, nonsteroidal anti-inflammatory drugs, and theophylline) were not included. Patients who had a history of thyroid disease, systemic sclerosis, systemic lupus erythematosus, or severe psychological disorders or were pregnant, breastfeeding, or planning to become pregnant were not eligible to take part in the study. Before participating, all patients were required to sign written informed consent.

All the participants were given the placebo treatment for 1 week. After the treatment, the symptoms were evaluated and the patients with the symptom improvement <50% were finally involved in the random treatment period.

Material

The Qi-Zhi-Wei-Tong granules used in the study were a commercially available preparation (2.5 g/package) (Beimao Natural Medicine Management Co., Ltd., Beijing, China). The placebo was designed by the company with 5% of the active ingredients of the medicine with the same label and had a similar taste, appearance, and smell, without having the same pharmacologically active effect as the treatment medicine. The patients were asked to take one pack of the medicine or placebo three times a day.

Study design

This was a randomized, double-blind, multicenter, placebo-controlled trial that included three phases. The first phase was a placebo run-in period (−7 to 0 day), during which patients who were eligible for the inclusion and exclusion criteria of the screening period were all treated with placebo for 1 week. Then, their symptoms were evaluated, and patients with symptoms that improved by more than 50% were considered to present the placebo effect and were excluded. In the next treatment period, patients who met the inclusion criteria of the treatment period were randomly (in a 1:1 ratio) assigned to 4 weeks of double-blinded treatment with Qi-Zhi-Wei-Tong granules (treatment group) or placebo (control group). The therapeutic effect and safety of patients were evaluated at weeks 2 and 4 after the medicine was taken. During the third period (follow-up period), patients were followed up to assess the symptoms and adverse events 2 weeks after the cessation of treatment. The whole process of the clinical trial is summarized in Figure 1.

Assessment

The patients used diary cards to record their symptoms and assessed the symptoms with investigators by means of a rating scale which was scored on a 5-point scale [Table 1] at baseline,[9-11] at weeks 2 and 4 after the start of treatment, and 2 weeks after the cease of the treatment. The rating scale consists of the degree and frequency of the two main

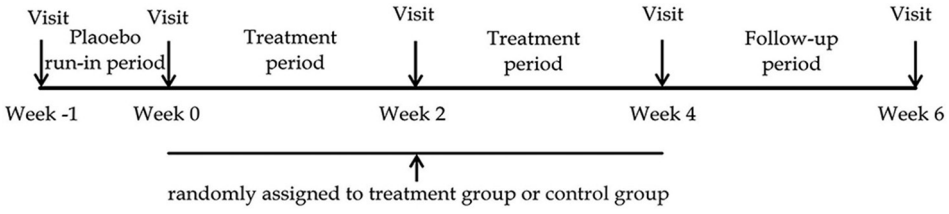

Figure 1: Study design.

Table 1: Rating scale

Score	Symptoms severity	Frequency
0	Absent	Absent
1	Mild, awareness of symptoms but can be easily ignored	1 day/week
2	Moderate, awareness of obvious symptoms but does not interfere with normal activities	2–3 days/week
3	Severe, awareness of obvious symptoms and interferes with normal activities	4–5 days/week
4	Extremely severe, awareness of obvious symptoms and tremendously influences daily activities	Happened almost every day or persistently

symptoms of FD (postprandial fullness and early satiety), and the global symptom index, for each symptom and for the total score, was obtained by multiplying severity by frequency.[12]

According to the Guideline for Directing Clinical Research into Treatment of Distention and Fullness with New Chinese Drugs, the curative effect was divided into four grades: clinical control refers to the disappearance of symptoms and an accumulated score of symptoms that was reduced by ≥95%; obvious effectiveness means that the symptoms improved and that the accumulated score was reduced by more than 75%; effectiveness means that the symptoms improved and that the accumulated score was reduced by 50–75%; and invalidation means that symptoms were aggravated or that the symptom improvement rate was improved by <50%.[13-15]

The formula for assessing the symptom improvement included the following: (1) symptom improvement rate = ([accumulated score before treatment − accumulated score after treatment]/accumulated score before treatment) × 100%; (2) total effective rate = ([clinical control cases + obvious effectiveness cases + effectiveness cases]/total cases) × 100%.

The primary outcome variable was the total curative rate at week 4. The second endpoint variables included the curative rate at week 2 and at follow-up observation, changes in dyspeptic symptom score at weeks 2 and 4 and at follow-up observation, and the anxiety/depression score as evaluated by the Zung Self-Rating Anxiety Scale (SAS) and Zung Self-Rating Depression Scale (SDS).[16,17]

Safety monitoring

All adverse events were required to be reported to the study coordinator in detail during the trial. Laboratory testing (routine blood test, routine urine test, and blood biochemistry examination), endoscopy, and abdominal ultrasound were performed before enrollment. Heart rate, blood pressure, physical examination, and electrocardiogram (ECG) were also conducted before enrollment and immediately after the treatment period.

Randomization and blinding

Randomization was done electronically by assigning patients a number corresponding to either Qi-Zhi-Wei-Tong granules or placebo (at a 1:1 ratio) in ascending order. Each randomization number was placed in a sequentially numbered opaque envelope that was sealed by the clinical research coordinator. After screening, the clinical investigator assigned the participants to a treatment group according to the randomization number. Both the investigators and patients were blinded to the assigned treatment throughout the study.

Sample size

The sample size was based on the superiority design as follows: $\alpha = 0.05$, $\beta = 0.20$, $P_T = 0.70$ (T: treatment group), and $P_C = 0.55$ (C: control group). The calculation indicated that a sample size of 161 would be sufficient. To allow for a 20% dropout rate and the need for random encoding blinding, we recruited 99 patients to the treatment group and 98 patients to the placebo group.

Statistical analysis

The measurement outcomes were assessed using the full analysis set (FAS) and the per-protocol set (PPS). The FAS included all patients randomized who received at least one dose of treatment (Qi-Zhi-Wei-Tong granules or placebo) and had valid data. A PPS analysis was also conducted and was limited to patients who completed at least the 4-week intervention, according to the protocol, without severe delay, and who had not taken any prohibited concomitant medications. The safety analysis set (SS) included data from patients who received at least one dose of treatment as well as a safety evaluation. The PPS was used in the efficacy evaluation, while the FAS and the SS were used in the safety evaluation.

All data were analyzed with SAS software (version 9.1; SAS Institute, USA). Quantitative variables are present as the mean ± standard deviation. Categorical variables were compared between groups with Chi-square test or Fisher's exact test. Continuous variables were compared with independent *t*-test between treatment groups. For in-group

comparisons, Paired *t*-test was performed. Two-sided $P < 0.05$ was considered statistically significant.

Results

Patient characteristics

A total of 197 PDS patients who met the enrollment criteria were included in the treatment period and were randomly divided into a treatment group (n = 99) and a control group (n = 98). Ten participants dropped out the study, but they received treatment and underwent at least three observation points. Therefore, the FAS and SS population was 197, with 99 in the treatment group and 98 in the control group. Data from 165 participants were included in the PPS analysis, with 85 in the treatment group and 80 in the control group. Reasons for exclusion from the PPS analysis are shown in Figure 2.

Mean height, weight, gender, age, marital status, previous medication use, previous medical history, vital signs, abdominal ultrasound, electrocardiogram, and gastroscopy showed no differences between the two groups ($P > 0.05$) [Table 2].

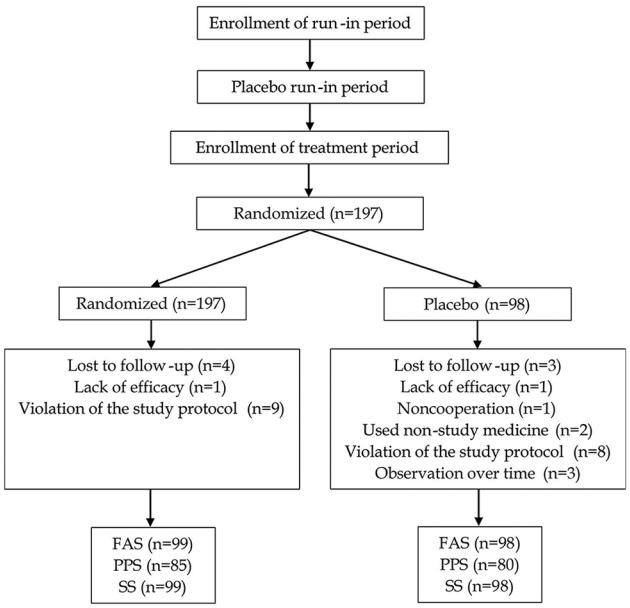

Figure 2: Flow diagram of patients progress through the RCT phases. RCT: Randomized controlled trial.

Primary outcome

Comparison of total effective rate of dyspeptic symptoms between the treatment and control group at week 4

After the 4-week treatment, the total effective rate in the treatment group (69.41% [59/85]) was significantly higher than that in the placebo group (16.25% [13/80]) ($\chi^2 = 49.13$, $P < 0.001$) [Table 3].

Secondary outcomes

Comparison of total effective rate of dyspeptic symptoms between the treatment and control group at week 2 and follow-up observation

The total effective rates in the treatment group at week 2 and the follow-up period were all significantly higher than those in the control group ($P < 0.001$) [Table 3].

Comparison of total gastrointestinal symptom scores between the treatment and control groups

The total gastrointestinal symptom scores in the treatment group at weeks 2 and 4 and follow-up observation were significantly lower than those in the control group in the PPS analysis ($P < 0.001$) [Table 4].

Comparison of severity and frequency of every dyspeptic symptom in postprandial distress syndrome between treatment and control group

Figure 3 shows the severity and frequency of the main dyspeptic symptoms (postprandial fullness and early satiety) before and after the treatment. In the treatment group, the severe and frequent proportions of postprandial fullness symptoms at weeks 2 and 4 after the treatment with Qi-Zhi-Wei-Tong granules and follow-up observation were significantly lower than those in the control group and at week 0 in PPS ($P < 0.001$) [Figure 3a and 3b]. The severity and frequency of early satiety symptoms at follow-up observation in the treatment group were also significantly lower than that in the control group and at week 0 in the PPS ($P < 0.001$) [Figure 3c and 3d].

Table 2: Baseline characteristics of patients with PDS

Characteristics	Control group (n = 98)	Treatment group (n = 99)
Height (cm) (mean ± SD)	163.38 ± 6.94	162.30 ± 16.42
Weight (kg) (mean ± SD)	58.64 ± 9.74	56.66 ± 9.46
Gender (male:female)	31:67	44:55
Age (years)	42.65 ± 10.61	40.87 ± 11.96
Marital status (single:married)	6:92	8:91
Previous medication use (no:yes)	5:93	2:97
Previous medical history (no:yes)	9:89	7:94
Vital signs		
Systolic pressure (mmHg)	114.73 ± 12.27	115.79 ± 9.51
Diastolic pressure (mmHg)	76.20 ± 24.60	75.73 ± 7.59
Heart rate (beats/min)	74.94 ± 9.80	77.11 ± 9.39
Abdominal ultrasound (abnormal:normal)	16:82	12:87
Electrocardiogram (abnormal:normal)	11:87	7:92

PDS: Postprandial distress syndrome; SD: Standard deviation.

Table 3: Comparison of total effective rate of Qi-Zhi-Wei-Tong granules on PDS (PPS) between treatment and control groups

Items	Week 2		Week 4		Follow-up	
	Control group	Treatment group	Control group	Treatment group	Control group	Treatment group
Clinical control	0	5 (5.88)	2 (2.50)	19 (22.35)	6 (7.50)	33 (38.82)
Obvious effectiveness	0	3 (3.53)	1 (1.25)	8 (9.41)	1 (1.25)	6 (7.06)
Effectiveness	7 (8.75)	25 (29.41)	10 (12.50)	32 (37.65)	10 (12.50)	27 (31.76)
Invalidation	73 (91.25)	52 (61.18)	67 (83.75)	26 (30.59)	63 (78.75)	19 (22.35)
Total effective rate (%)	8.75	38.82	16.25	69.41	21.25	77.65
P	<0.001		<0.001		<0.001	

Data are expressed as frequencies and percentages. PPS: Per-protocol set; PDS: Postprandial distress syndrome.

Table 4: Comparison of overall gastrointestinal symptom scores in PDS over the trial period (PPS)

Group	Week 0	Week 2	Week 4	Follow-up
Control	8.46 ± 2.90	8.06 ± 3.20	7.23 ± 3.38	7.21 ± 3.85
Treatment	9.56 ± 3.22	5.73 ± 3.10*,†	3.87 ± 3.12*,†	2.98 ± 3.20*,†

Data are expressed as the mean ± SD. *P<0.001 versus the control group; †P<0.001 versus week 0. SD: Standard deviation; PPS: Per-protocol set; PDS: Postprandial distress syndrome.

Changes of Zung Self-Rating Anxiety Scale and Zung Self-Rating Depression Scale

At baseline, there was no significant difference between the treatment and control groups. After 4 weeks of treatment and the follow-up period, the SAS scores in the treatment group were significantly lower than those in the control group ($P < 0.001$) in the PPS [Table 5]. Nevertheless, there was no significant difference in SDS scores between the two groups at week 4 and at the follow-up observation in the PPS ($P > 0.05$) [Table 5].

Safety analysis

During the treatment period, there were no serious adverse events in either group. In the treatment group, one PDS patient reported mild elevation of cholesterol, and one suffered from a mild dry mouth. In the control group, two patients reported side effects: one reported mild constipation and the other reported moderate elevation of urinary protein. The incidence of adverse events was 3.03% and 3.06% in the treatment and control groups, respectively ($P > 0.05$).

Discussion

In this double-blind, placebo-controlled randomized trial, compared with placebo treatment, 4 weeks of treatment with Qi-Zhi-Wei-Tong granules yielded statistically and clinically significant improvements in gastrointestinal symptoms associated with PDS as well as anxiety. Two weeks after the cessation of treatment, the beneficial effect of Qi-Zhi-Wei-Tong granules was sustained, and there were continued improvements in anxiety to some degree. These results lend support to the use of Qi-Zhi-Wei-Tong particles for FD as a valuable and reliable option.

The placebo effect is a common phenomenon in FD treatment and is reported to reach proportions as high as 13–73%.[18,19] Furthermore, herbals have a special taste, appearance, and smell, which make it hard to exclude the placebo effect. Previously, most herbal trials were performed with open-labeled methods.[20-23] In the present study, we designed the placebo, which contained 5% of the active ingredient of the medicine, to have a similar taste, appearance, and smell without having a pharmacologically active effect. In the recruitment period, the patients who positively reacted to the placebo were excluded, which could effectively avoid the placebo effect.

The appropriate treatment duration for functional gastrointestinal disorders is still not well defined. Some investigations suggested that an 8–12-week duration can prevent the placebo effect well.[24] In the present trial, we designed the treatment duration to be 4 weeks since patients might take the medicine on demand in long-term studies and increase the possibility of bias.

One of the likely infectious causes of FD is *Helicobacter pylori*, and it appears plausible that the eradication of *H. pylori* could benefit patients with FD. However, we did not perform an *H. pylori* urease breath test or blood ELISA antibody test before the recruitment of patients; this decision was made because whether *H. pylori* is a cause of FD is not well established, and the benefits of *H. pylori* eradication in the treatment of FD are limited. In addition, it has been shown that symptoms of epigastric pain and epigastric burning were more likely to improve with *H. pylori* treatment compared to placebo, but symptoms in PDS (postprandial fullness, early satiety, nausea, and belching) did not improve.[25]

Our data suggested that Qi-Zhi-Wei-Tong granules could effectively decrease both the overall symptom score and the frequency/severity of the symptoms of early satiety or fullness. The mechanisms of FD involve a series of pathophysiological abnormalities, including delayed gastric emptying, impaired accommodation, and visceral hypertension. Several studies reported that delayed gastric emptying was present in as high as 50% of FD patients and was correlated with the symptom of fullness.[26-28] Therefore, prokinetic medicines are the main agent used in the treatment of FD, especially in the PDS subtype.[29] Unfortunately, current commercially available prokinetics have some potential adverse effects, including severe arrhythmia, which limit their clinical use.[30]

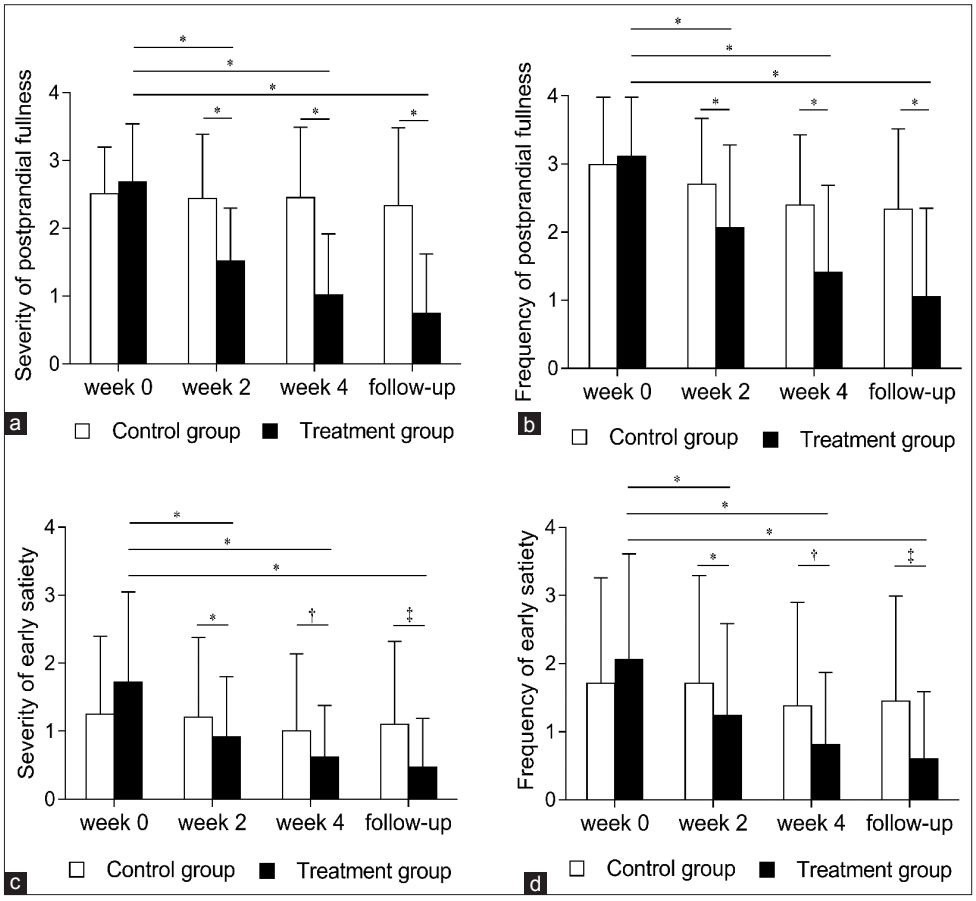

Figure 3: Comparison of the severity and frequency of dyspeptic symptoms between the treatment and control groups. (a and b) showing that the severity and frequency of postprandial fullness at weeks 2 and 4 and the follow-up period were all significantly lower than those in the control group and week 0. *$P < 0.001$. (c and d) showing that the severity and frequency of early satiety at weeks 2 and 4 and the follow-up period were all significantly lower than those in the control group and week 0. *$P < 0.05$, †$P < 0.01$, ‡$P < 0.001$.

Table 5: Changes in SAS and SDS scores in PDS over the trial period (PPS)

Scales	Week 0		Week 4		Follow-up	
	Control group	Treatment group	Control group	Treatment group	Control group	Treatment group
SAS	75.93 ± 13.43	72.06 ± 12.93	74.91 ± 14.18	68.20 ± 9.53†	73.78 ± 14.80	68.19 ± 9.70*
SDS	47.25 ± 13.42	47.05 ± 13.42	47.28 ± 13.24	45.49 ± 13.51	47.60 ± 13.80	46.33 ± 14.04

Data are expressed as the mean ± SD. *P<0.01; †P<0.001 versus the control group. SAS: Self-rating anxiety scale; SDS: Self-rating depression scale; PPS: Per-protocol set; PDS: Postprandial distress syndrome; SD: Standard deviation.

Although the mechanisms of Qi-Zhi-Wei-Tong granules on accelerating gastric emptying are still unclear, previous studies have shown that the contents of the medicine have an effect on gastric motility and visceral sensation. Jiang *et al*. reported that Fructus Aurantii could increase the intensity of vasoactive intestinal peptide and serotonin in the gastrointestinal wall and enhance the gastrointestinal motility.[31] Fang *et al.*'s study showed that Radix Paeoniae Alba and Fructus Aurantii Immaturus regulated the gastrointestinal motility in bilateral effect via the H1 histamine receptor, nuclear factor-kappa B p65 translocation and production.[32] In addition, Lin *et al*. reported an analgesic and sedative effect of *Corydalis* via the hypothalamus serotonin pathway.[33] Other than the subjective treatment effect, our data showed much higher beneficial effects of Qi-Zhi-Wei-Tong granules than the traditional medicine in the treatment of FD.[34] In our run-in period, we treated patients with the placebo, and the patients who reacted well to the placebo were excluded. This procedure minimized the possible placebo effect, which might contribute to the positive treatment effect of Qi-Zhi-Wei-Tong granules.

The present study also suggested that Qi-Zhi-Wei-Tong granules decreased the anxiety score. Anxiety and depression are commonly present in FD and may aggravate the symptoms.[35] Recent studies have shown that psycho-pharmaco-therapy could effectively relieve the symptoms of FD.[36] In the present study, our data showed that the anti-anxiety effect in the off-treatment period tends to fall

off, although the gastrointestinal symptom relief was still sustained. This phenomenon suggested that the decrease in anxiety/depression score might contribute to the anti-anxiety effect of the Qi-Zhi-Wei-Tong granules, but not to the relief of gastrointestinal symptoms. The anti-anxiety effect of Qi-Zhi-Wei-Tong granules is still unclear. The component of *Corydalis* has been shown to have a sedative effect via the dopaminergic and GABAergic neurons in the amygdala, which might contribute to its effects.[37,38] The mechanism of Qi-Zhi-Wei-Tong granules on improving anxiety and depression still requires further study.

The primary limitation of this study was that we could not ascertain the long-term efficacy after treatment with Qi-Zhi-Wei-Tong granules for FD. Further investigation would be necessary to confirm and resolve this issue.

In conclusion, our data suggest that Qi-Zhi-Wei-Tong granules are superior to placebo in the treatment of the PDS subtype of FD. The medicine shows effects on the main gastrointestinal symptoms and psychological disorders in PDS. The precise mechanisms of action need to be elucidated.

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Conflicts of interest

There are no conflicts of interest.

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气滞胃痛颗粒治疗功能性消化不良餐后不适综合征疗效与安全性的多中心、随机、双盲、安慰剂对照临床试验

摘要

背景：功能性消化不良是一种常见的上消化道功能性疾病，目前对于其药物治疗效果仍欠满意。本文旨在评估气滞胃痛颗粒对功能性消化不良的餐后不适综合征亚型的临床疗效与安全性。

方法：采用随机、双盲、多中心、安慰剂对照的方法观察餐后不适综合征患者197例。对所有入组患者给予1周安慰剂治疗，1周后症状积分下降不大于50%的患者将被随机分配到气滞胃痛颗粒组或安慰剂组，2组治疗疗程均为4周，治疗结束后2周再次进行随访。在第0，2，4周和治疗结束后2周观察记录两组临床症状的改善情况，并采用Zung氏焦虑/抑郁自评量表（SAS/SDS）在第0，4和治疗结束后2周评估患者心理状态。

结果：在第2，4周和治疗结束后2周，气滞胃痛颗粒组的总有效率（38.82%，69.14%，77.65%）均高于安慰剂组（8.75%，16.25%，21.25%），差异有统计学意义（P均< 0.001）;在第2，4周和治疗结束后2周，气滞胃痛颗粒组的症状积分低于安慰剂组，差异有统计学意义（P < 0.001）;在第2，4周和治疗结束后2周，气滞胃痛颗粒组的单症状（餐后饱胀不适、早饱）严重程度与频率均分别低于安慰剂组，差异有统计学意义（P < 0.05）;在第4周和治疗结束后2周，气滞胃痛颗粒组的SAS评分低于安慰剂组，差异有统计学意义（P < 0.001）;气滞胃痛颗粒组和安慰剂组均未发现严重不良事件，不良事件出现率为3.03%与3.06%，差异无统计学意义（P > 0.05）。

结论：气滞胃痛颗粒治疗餐后不适综合征的综合疗效显著、稳定，无明显不良反应。