Chin J Integr Med 2013 Jul;19(7):498-504

ORIGINAL ARTICLE

Efficacy of Gastrosis No.1 Compound on Functional Dyspepsia of Spleen and Stomach Deficiency-Cold Syndrome: A Multi-Center, Double-Blind, Placebo-Controlled Clinical Trial*

ZHANG Sheng-sheng (张声生)[1], ZHAO Lu-qing (赵鲁卿)[1], WANG Hong-bing (汪红兵)[1], WU Bing (吴 兵)[1], WANG Chui-jie (王垂杰)[2], HUANG Sui-ping (黄穗平)[3], SHEN Hong (沈 洪)[4], WEI Wei (魏 玮)[5], and LAI Yao-liang (来要良)[6]

ABSTRACT **Objective**: To assess the efficacy and safety of Gastrosis No.1 compound in the treatment of functional dyspepsia with Spleen (Pi) and Stomach (Wei) deficiency-cold syndrome. **Methods**: A randomized, double-blind, placebo-controlled trial was performed in 5 centers. Patients with functional dyspepsia (FD) of Spleen-deficiency and qi-stagnation syndrome (162 cases) were randomly assigned to groups given Chinese herbal medicine (CHM) Gastrosis No.1 compound or placebo in a 2:1 ratio. This trial included a 4-week treatment period and a 4-week follow-up period. The outcomes were the dyspepsia symptom scores (measured by total dyspepsia symptom scale and single dyspepsia symptom scale) and syndromes of traditional Chinese medicine score (measured by traditional Chinese medicine syndrome scale). The outcomes were noted at weeks 0, 4 and 8. **Results**: Compared with patients in the placebo group, patients in the CHM group showed significant improvement in the dyspepsia symptom scores as rated by patients and investigators ($P<0.01$), and also showed improvement in syndromes of traditional Chinese medicine score ($P<0.01$). No serious adverse event was reported. Safety tests obtained after 4 weeks of treatment showed no abnormal values. **Conclusion**: CHM Gastrosis No.1 compound was effective and safe in the treatment of functional dyspepsia with Spleen and Stomach deficiency-cold syndrome.

KEYWORDS functional dyspepsia, Spleen and Stomach deficiency-cold syndrome, randomized controlled trial

Functional dyspepsia (FD) is a common functional gastrointestinal disorder characterized by chronic or recurrent upper abdominal fullness, epigastric pain, belching, bloating, early satiety, nausea, vomiting, regurgitation, burning, loss of appetite, and other symptoms. FD accounts for a significant proportion of patients seen in gastroenterology offices. The global prevalence of FD is estimated between 11.5% and 29.2%.[1-4] The direct and indirect economic burden caused by FD is huge and has considerable negative impact on productivity.[5,6] The pathophysiology of FD is poorly understood, although various mechanisms are thought to play a role in the development of symptoms.[7-10] No single available treatment is reliably effective for this condition. Many studies have suggested the potential effectiveness of Chinese herbal medicine (CHM) in the treatment of FD,[11] but most of the previous clinical trials lacked rigor design and used poor techniques for randomization and blinding. To date, no strong scientific evidence supporting the use of CHM in FD is available.

In this trial, we aimed to test the efficacy of the Gastrosis No.1 compound in patients with FD and Spleen (Pi) and Stomach (Wei) deficiency-cold syndrome using a randomized, double-blind, placebo-controlled study design.

METHODS

Study Design

This study was a double-blind, placebo-controlled clinical trial. Patients were randomized into CHM or

*Supported by the Eleventh Five-Year National Key Technology R&D Program (No. 2007BAI20B092)

1. Beijing Hospital of Traditional Chinese Medicine Affiliated to Capital Medical University, Beijing (100010), China; 2. The Affiliated Hospital of Liaoning University of Traditional Chinese Medicine, Shenyang (110033), China; 3. The Second Affiliated Hospital of Guangdong University of Traditional Chinese Medicine, Guangzhou (510120), China; 4. The Affiliated Hospital of Nanjing University of Traditional Chinese Medicine, Nanjing (210029), China; 5. Wangjing Hospital, China Academy of Chinese Medical Sciences, Beijing (100102), China; 6. Beijing Xuanwu Hospital of Traditional Chinese Medicine, Beijing (100050), China
Correspondence to: Prof. ZHANG Sheng-sheng, Tel: 86-10-52176720, E-mail: zhss2000@163.com

DOI: 10.1007/s11655-013-1503-x

placebo groups in a 2:1 ratio. Because it would be unethical to assign an equal number of ill subjects to the ineffective placebo treatment, the 2:1 randomization plan was chosen to protect the rights of the subjects. The trial protocol was approved by regional ethics review boards, including the National Review Board for Clinical Drug Research in the Beijing Hospital of Chinese Medicine Hospital Affiliated to Capital Medical University. There were no major changes in the study protocol after initiation of the study.

Participants

Patients were screened by investigators at five sites in China: the Beijing Hospital of Traditional Chinese Medicine Affiliated to Capital Medical University (60 cases), the Affiliated Hospital of Liaoning University of Traditional Chinese Medicine (36 cases), the Second Affiliated Hospital of Guangdong University of Traditional Chinese Medicine (36 cases), the Affiliated Hospital of Nanjing University of Traditional Chinese Medicine (12 cases), and the Beijing Xuanwu Hospital of Traditional Chinese Medicine (18 cases). Patients were assessed according to the Rome Ⅲ criteria[12] and the Guiding Principle for Clinical Research on New Drugs of Traditional Chinese Medicine.[13] Written informed consents were obtained from all patients prior to inclusion in the trial. Patients were free to withdraw from the study at any time.

Inclusion Criteria

(1) Patients who meet the Rome Ⅲ diagnosis standard of FD. (2) Patients who have Spleen and Stomach deficiency-cold syndrome. (3) Patients aged 18 to 65 without gender limitation and (4) signed the informed consent.

Exclusion Criteria

(1) Patients who combined with gastrointestinal ulcer, erosive gastritis, atrophic gastritis, severe dysplasia of gastric mucosa or suspicious malignant lesion. (2) Patients who have overlap syndrome combined with gastroesophageal reflux disease or irritable bowel syndrome. (3) Patients whose syndrome is difficult to differentiate. (4) Patients who have connective tissue diseases, diabetes or other endocrine disease, climacteric syndrome, or severe diseases in heart, liver, lung, kidney, blood. (5) Pregnant or lactating women, disabled people. (6) Patients with history of alcoholic or drug abuse. (7) Patients who have allergic constitution or known to be allergic to the drug used in this trial. (8) Patients who are involved in other trials. (9) Patients with poor compliance or other reasons that the researcher considered not to be appropriate to participate in this trial. (10) Patients with severe depression and have suicidal tendency.

Interventions

Patients in CHM group were provided granules of Chinese herbal extracts, which were prepared by Tcmages Pharmaceutical Co., Ltd. (Beijing, China). The standard herb formula (Table 1) was a Gastrosis No.1 compound. Patients in the placebo group were given placebo granules, which were prepared by the same supplier and were designed with taste, smell and look similar to the Chinese herbal formula granules. Granules were dissolved in 300 mL boiled water cooled to 70 ℃. Patients in both groups were required to take 150 mL (50 ℃) twice daily. For the duration of the trial, the patients were not allowed to take any concomitant medications associated with the treatment of FD. Treatment continued for 4 weeks and was followed by a 4-week follow-up period.

Table 1. Chinese Herbal Formula

Chinese name	Pharmaceutical name	Powdered herb (%)
Dangshen	Pilose Asiabell Root	19.05
Baizhu	Largehead Atractylodes Rhizoma	14.29
Ganjiang	Dried Ginger	9.52
Gancao	Liquorice Root	4.76
Sugeng	Perilla Stem	9.52
Houpo	Cortex Mangnoliae officinalis	9.52
Shenqu	Medicated Leaven	14.29
Bibo	Piper longum	9.52
Xiangfu	Rhizoma cyperi	9.52

Outcomes

Primary outcome

The FD symptoms were assessed using two scales: (1) the total dyspepsia symptom (TDS) scale and (2) the single dyspepsia symptom (SDS) scale. Ratings were completed by both the investigators and patients at baseline and at weeks 1, 2, 3, 4 and 8.

TDS Scale

TDS scale consisted of the assessment of eight items (postprandial fullness and bloating, early satiety, epigastric pain, epigastric burning, nausea, vomiting, belching and "other symptoms"), each with four

options (absent=0, mild=1, moderate=2, or severe=3).

SDS Scale

The SDS scale measured three aspects of four principal symptoms of FD. The symptoms were epigastric pain, epigastric burning, postprandial fullness and bloating, and early satiety. The three aspects were the frequency, intensity and level of discomfort, and were rated by four options (absent=0, mild=1, moderate=2, or severe=3). The total score obtained using this scale was called the SDS score.

The Secondary Outcome

Chinese Medicine Syndrome Scale

The Chinese medicine syndrome (CMS) scale consisted of the assessment of ten items (abdominal heaviness, epigastralgia, lack of appetite, hiccup, dryness bitterness of the mouth, fatigue and weakness, nausea and vomiting, noisy, chest congestion, somatic heaviness and sleepy), each with four options (absent=0, mild=3, moderate=6, severe=9) or (absent=0, mild=2, moderate=4, severe=6).

Safety Monitoring

To assess the safety of the 4-week treatment, routine tests of blood, urine and stool samples, as well as electrocardiogram (ECG) and blood biochemical tests alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), serum creatinine (SCr), were conducted before randomization and immediately after the completed treatment. During the trial, adverse events were observed in detail and documented using case report forms (CRFs).

Sample Size

The sample size was calculated in two ways. To guarantee the reliability of the trial, the calculation yielding the larger sample size was used. The sample size was calculated according to the following formula:[14]

$$n_1=\frac{[u_a\sqrt{p_c(1-p_c)(1+c)/c}+u_b\sqrt{p_1(1-p_1)+p_2(1-p_2)/c}]^2}{(p_1-p_2)^2}$$

$n_2=cn_1$

n_1CHM, $n_2$placebo

$p_c=\frac{p_1+cp_2}{1+c}$, $u_a=1.64$, $u_b=1.28$, $c=2$, $p_1=0.5$, $p_2=0.75$

The patients were assigned to either the CHM group or the placebo group (in a 2:1 ratio). The effective rates of treatment and placebo were assumed to be 75% and 50%, respectively.[15,16] The calculation indicated that a sample size of 138 would be sufficient (n=92 in the treatment group, n=46 in the control group). To allow for a 15% rate of dropouts and missing data, we recruited 108 patients for the treatment group and 54 patients for the control group.

Randomization and Blinding

Randomization was performed with SAS9.10. Eligible patients were assigned a randomization number according to a predetermined list by investigators at each center. These numbers were allocated to patients in sequential order and registered in the patient enrollment list and the allocation was concealed. Emergency envelopes containing the randomization code were provided to the investigators and were examined at the end of the trial to ensure that the blinded conditions had been maintained.

Statistical Analysis

Intention to treat (ITT) analysis was used, using all available data at each time point and the baseline observation carried forward (BOCF) approach for missing data. The statistical analysis was performed by the Center of Clinical Epidemiology of the Third Hospital of Peking University. Parametric Student's t-test or non-parametric Wilcoxon test was used to quantitatively compare variables, according to distribution characteristics. Quantitative variables are reported as mean ± standard deviation. Statistical significance was considered at $P<0.05$.

RESULTS

Study Population

Between April 2009 and March 2011, a total of 162 patients were recruited: 108 were randomized into the CHM group and 54 into the placebo group. Two patients withdrew from the trial due to a lack of efficacy. No adverse events were reported. The physiological tests obtained after 4 weeks of treatment showed no abnormal values.

Participant Flow

The flow of participants in the study is summarized in Figure 1.

Baseline Data

No significant differences were identified between the two groups in parameters such as

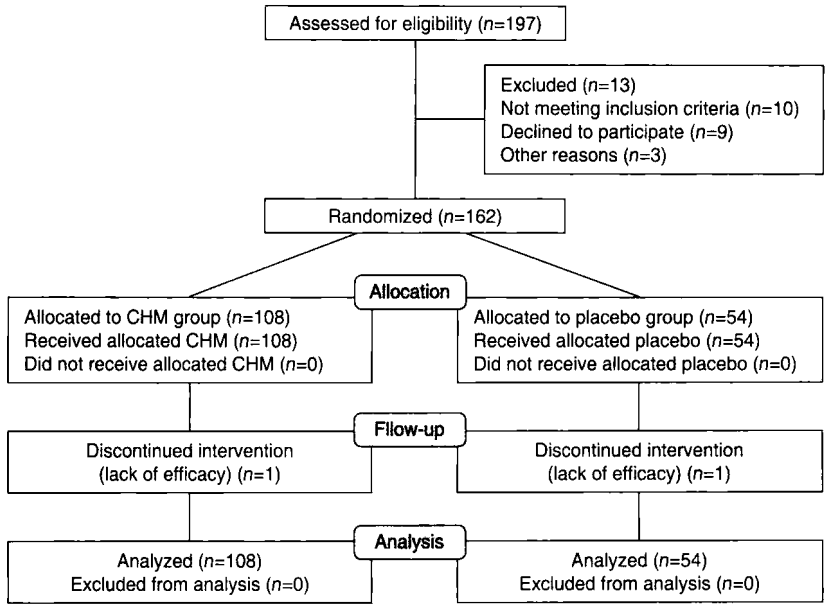

Figure 1. The Flow of the Participants in the Study

gender, age, course of disease or symptom scores before treatment (Table 2).

Table 2. Characteristic and Baseline Data of Two Groups

Variables	CHM (*n*=108)	Placebo (*n*=54)	*P* values
Characteristic			
Age (year)	35.87 ± 10.72	37.50 ± 11.41	
Sex ratio (male:female)	38:70	17:37	
Height (cm)	165.34 ± 7.12	164.15 ± 6.21	
Weight (kg)	59.77 ± 10.56	60.32 ± 12.25	
Course of disease (month)	42.67 ± 54.41	39.68 ± 48.71	
Baseline data (week 0)			
Gastroenterologist TDS scores	6.06 ± 2.77	5.67 ± 2.40	
Patient TDS scores	6.13 ± 2.68	5.72 ± 2.38	
Gastroenterologist SDS scores			
epigastric pain	3.87 ± 2.33	3.80 ± 1.94	*P*>0.05
epigastric burning	0.74 ± 1.44	0.43 ± 1.14	
postprandial fullness and bloating	4.47 ± 2.09	3.94 ± 2.76	
early satiety	2.61 ± 2.06	2.48 ± 2.18	
Patient SDS scores			
epigastric pain	3.89 ± 2.35	3.81 ± 1.95	
epigastric burning	0.74 ± 1.44	0.46 ± 1.16	
postprandial fullness and bloating	4.43 ± 2.31	3.89 ± 2.36	
early satiety	2.69 ± 2.01	2.61 ± 2.25	
CMS scores	20.03 ± 9.19	19.22 ± 9.42	

Primary Outcome Variables

TDS Scale

After 4 weeks of treatment, the TDS score assessed by investigators was significantly better for the CHM group than for placebo (Z=–3.770, *P*<0.01). At week 8, the score was also significantly better for CHM than for placebo (Z=–3.714, *P*<0.01). The TDS scores provided by the patients themselves were similar to those given by the investigators (Table 3).

The results were clinically meaningful. Ratings of the clinical global impression of improvement after the treatment showed the following significant results for the treatment group *vs.* placebo group: very much improved (56.5% *vs.* 25.9%), much improved (14.8% *vs.* 20.4%), small improvement (20.4% *vs.* 22.2%), and unchanged or deterioration (8.3% *vs.* 31.5%, *P*<0.01).

SDS Scale

SDS scores assessed by investigators: After 4 weeks of treatment, the scores of postprandial fullness and bloating, early satiety, and epigastric pain were significantly better for the CHM group than for placebo (*P*<0.01). The score of burning sensation was not different between the two groups (*P*>0.05). At week 8, the scores of postprandial fullness and bloating, early satiety, and epigastric pain were significantly better for CHM than for placebo (*P*<0.01 or *P*<0.05). The score of burning sensation was not different between the two groups (*P*>0.05, Table 3).

The SDS scores provided by patients were similar to those given by investigators.

The Secondary Outcome

CMS Scale

After 4 weeks of treatment, the CMS score assessed by investigators was significantly better for the CHM group than for placebo (Z=–3.779, *P*<0.01). At week 8, the score was also significantly better for CHM than for placebo (Z=–3.730, *P*<0.01, Table 3).

The results were clinically meaningful. Ratings of the clinical global impression of improvement after the treatment showed the following significant results for the treatment group *vs.* placebo group: very much improved (30.6% *vs.* 11.1%), much improved (30.6% *vs.* 18.5%), small improvement (30.6% *vs.* 35.2%), and unchanged or deterioration (8.3% *vs.* 35.2%, *P*< 0.001).

Table 3. TDS , SDS and CMS Scores between Two Groups

Variables	CHM (*n*=108)	Placebo (*n*=54)	*P* values
Week 4			
Gastroenterologist TDS scores	1.62 ± 1.85	3.02 ± 2.38	<0.01
Patient TDS scores	1.62 ± 1.85	3.02 ± 2.38	<0.01
Gastroenterologist SDS scores			
epigastric pain	0.90 ± 1.62	1.63 ± 1.92	<0.01
epigastric burning	0.22 ± 0.86	0.09 ± 0.49	>0.05
postprandial fullness and bloating	1.26 ± 1.82	2.42 ± 2.09	<0.01
early satiety	0.46 ± 1.11	1.57 ± 1.83	<0.01
Patient SDS scores			
epigastric pain	0.90 ± 1.62	1.63 ± 1.92	<0.01
epigastric burning	0.22 ± 0.86	0.09 ± 0.49	>0.05
postprandial fullness and bloating	1.26 ± 1.82	2.42 ± 2.09	<0.01
early satiety	0.46 ± 1.11	1.57 ± 1.83	<0.01
CMS scores	5.10 ± 5.46	9.74 ± 7.84	<0.01
Week 8			
Gastroenterologist TDS scores	1.81 ± 1.93	3.11 ± 2.25	<0.01
Patient TDS scores	1.81 ± 1.98	3.07 ± 2.27	<0.01
Gastroenterologist SDS scores			
epigastric pain	0.90 ± 1.65	1.91 ± 2.08	<0.01
epigastric burning	0.22 ± 0.80	0.09 ± 0.49	>0.05
postprandial fullness and bloating	1.32 ± 1.76	2.67 ± 2.15	<0.01
early satiety	0.54 ± 1.11	1.15 ± 1.66	<0.05
Patient SDS scores			
epigastric pain	0.93 ± 1.67	1.89 ± 2.07	<0.01
epigastric burning	0.22 ± 0.80	0.09 ± 0.49	>0.05
postprandial fullness and bloating	1.34 ± 1.78	2.65 ± 2.15	<0.01
early satiety	0.56 ± 1.15	1.15 ± 1.66	<0.05
CMS scores	5.82 ± 5.85	10.48 ± 7.98	<0.01

Adverse Event

No serious adverse event was reported. Safety tests obtained after 4 weeks of treatment showed no significant abnormal values.

DISCUSSION

FD is a heterogeneous disorder. It involves many pathogenic factors and different pathophysiological disturbances, including delayed gastric emptying, impaired accommodation, and hypersensitivity to gastric distention. Treatment of the underlying pathophysiological abnormality seems logical, but the main pharmacotherapeutic options include acid suppression, prokinetic drugs, and antidepressants,[6,17-19] all of which have limited effects. Herbal formulations are widely used to treat FD in China and many other areas in the world. However, the available evidence of the efficacy of these formulas is inadequate.

This multi-center, randomized, double-blind, placebo-controlled study indicates that Gastrosis No.1 compound is effective in the management of symptoms associated with FD and gastric emptying. The effects appeared to last for up to 4 weeks after completion of treatment, and were particularly beneficial for postprandial fullness and bloating, early satiety, and epigastric pain. Patients receiving Gastrosis No.1 compound treatment demonstrated significantly better outcomes (both clinically and statistically) on all the outcome measures compared with patients receiving placebo. Moreover, no serious adverse events were reported during the study.

The evaluation of treatment effects in FD is difficult and there is currently no gold standard. In our study, we used two different parameters as the main target variables. The TDS scale included almost all symptoms associated with FD, and the SDS scale included information on the four principal symptoms of FD, measured in terms of the frequency, intensity and level of discomfort. The main target variables were recorded by both investigators and patients. We

also assessed CM syndromes by CMS scale. Another difficulty in clinical trials with patients with FD is the remarkable placebo response. It has been shown that one third of patients with FD will respond to placebo in short-term trials,[20] and the proportion may be even higher in long-term studies. In our study, we made a great effort to make the treatments in the two groups indistinguishable for the patients. A placebo of similar appearance, smell and taste to the active concoction was used. To ensure that the patients were not able to discriminate between placebo and active treatment, 20 healthy volunteers participated in a randomized taste and visual assessment of the placebo and active medication. Eight volunteers correctly identified the active compound as active, whereas twelve volunteers considered the placebo preparation to be the active compound. Thus, it is reasonable to assume that the medication was given in an appropriately blinded manner. Despite the well-known high response rate to placebo in FD, we found significantly greater improvements in dyspepsia symptoms and gastric emptying in patients receiving the CHM compared with placebo-treated patients.

In CM, injury by food or drink, emotional injury, and congenital defects are main pathogenic factors of FD. All these pathogenic factors cause abnormal function of the Spleen and Stomach. Spleen and Stomach deficiency-cold exist throughout the course of the disease. The herbal formula provided to patients in this study was Gastrosis No.1 compound. All the herbs matched well, and could strengthen the Spleen and Stomach. Because the function of the Spleen and Stomach recovered, all the dyspepsia symptoms were abated. This is in accordance with previous studies[21-25] which showed physiological effects of Lizhong Decoction (理中汤) and some other herbal medicines in the Gastrosis No.1 compound. However, herbal preparations are complex and contain a number of active ingredients that may work together. The multiple effects of different active ingredients may be of benefit for the variety of different symptoms that occur in functional gastrointestinal disorders. However, more studies are needed to explore the mechanisms of action and properties of the identified components. FD is a common, chronic and recurrent functional gastrointestinal disorder. This study used a short treatment period and follow-up and a relatively small number of patients, so there is ample room to enhance the evaluation of efficacy and safety by further studies.

We conclude that Gastrosis No.1 compound may offer symptomatic improvements in patients with FD. In this randomized, double-blind, placebo-controlled trial, Gastrosis No.1 compound was shown to be effective in the management of FD. Further studies are needed to determine the precise mechanisms of action.

Trial Registration

Chinese Clinical Trial Registry (ChiCTR): ChiCTR-TRC-10001074.

Acknowledgments

We thank the physicians in the five hospitals for their work in this study and the patients in our study for their participation.

Authors' Contributions

Prof. ZHANG Sheng-sheng, Dr. WANG Hong-bing, Dr. ZHAO Lu-qing and Dr. WU Bing contributed to the conception and design of the study. Prof. ZHANG Sheng-sheng and Dr. ZHAO Lu-qing drafted the manuscript. All authors contributed to further writing of the manuscript. All authors read and approved of the final manuscript.

Competing Interests

The authors declare that they have no competing interests.

REFERENCES

1. Shaib Y, El-Serag HB. The prevalence and risk factors of functional dyspepsia in a multiethnic population in the United States. Am J Gastroenterol 2004;99:2210-2216.
2. Bernersen B, Johnsen R, Straume B. Non-ulcer dyspepsia and peptic ulcer: the distribution in a population and their relation to risk factors. Gut 1996;38:822-825.
3. Hirakawa K, Adachi K, Amano K, Katsube T. Prevalence of non-ulcer dyspepsia in the Japanese population. J Gastroenterol Hepatol 1999;14:1083-1087.
4. Lu CL, Lang HC, Chang FY. Prevalence and health/social impacts of functional dyspepsia in Taiwan: a study based on the Rome criteria questionnaire survey assisted by endoscopic exclusion among a physical check-up population. Scand J Gastroenterol 2005;40:402-411.
5. Brook RA, Kleinman NL, Choung RS. Excess comorbidity prevalence and cost associated with functional dyspepsia in an employed population. Dig Dis Sci 2011;13:109-118.

6. Brook RA, Kleinman NL, Choung RS. Functional dyspepsia impacts absenteeism and direct and indirect costs. Clin Gastroenter Hepatol 2010; 8:498-503.
7. Tack J, Lee KJ. Pathophysiology and treatment of functional dyspepsia. J Clin Gastroenterol 2005;39(5 Suppl 3):S211-216.
8. Lee KJ, Tack J. Duodenal implications in the pathophysiology of functional dyspepsia. J Neurogastroenterol Motil 2010;16:251-257.
9. Zeng F, Qin W, Liang F. Abnormal resting brain activity in patients with functional dyspepsia is related to symptom severity. Gastroenterology 2011;141:499-506.
10. Savarino E, Zentilin P, Dulbecco P. The role of acid in functional dyspepsia. Am J Gastroenterol 2011;106:1168.
11. Zhang SS, Su DM, Zhao LQ. Systematic review on the efficacy of TCM in the treatment of functional dyspepsia. Chin J Integr Tradit West Med Digestion (Chin) 2011;23:32-34.
12. Rome Foundation. Guidelines–Rome Ⅲ diagnostic criteria for functional gastrointestinal disorders. J Gastrointestin Liver Dis 2006;15:307-312.
13. Zheng XY. Guiding principle of clinical research on new drugs of Chinese medicine in the treament of stuffiness and fullness. In guiding principle of clinical research on new drugs of Chinese medicine (trial implementation). Edited by: Yu XH. Bejing: Chinese Medical Science and Technology Press; 2002:54-58.
14. Liu X. Experimental design and data processing (fourth). Chin J Difficult Complicated Cases (Chin) 2003;2:55-57.
15. Zhang YP, Luo JH, Zhou C. The clinical curative effect of Jianpi Oral Liquid on 87 cases of Spleen and Stomach deficiency-weakness syndrome. Chin Tradit Patent Med (Chin) 1999;21:239-242.
16. Holtmann G, Talley NJ, Liebregts T, Adam B, Parow C. A placebo-controlled trial of itopride in functional dyspepsia. New Engl J Med 2006;354:832-840.
17. Oshima T, Miwa H. Treatment of functional dyspepsia: where to go and what to do. J Gastroenterol 2006;41:647-653.
18. Mönkemüller K, Malfertheiner P. Drug treatment of functional dyspepsia. World J Gastroenterol 2006;12:2694-2700.
19. Hojo M, Miwa H, Yokoyama. Treatment of functional dyspepsia with antianxiety or antidepressive agents: systematic review. J Gastroenterol 2005;40:1036-1042.
20. Talley NJ, Locke GR, Lahr BD. Predictors of the placebo response in functional dyspepsia. Aliment Pharmacol Ther 2006;23:923-936.
21. Zhao BG, Sun QF. Modern pharmacological studies and clinic application of Lizhong Bolus. Chin Tradit Patent Med (Chin) 2010;32:1957-1960.
22. Guo JC, Zhang AJ, Zheng XH, Zhou QF. Experimental study of complex Dangshen ventilation oral solution on intestinal function recovery after operation on abdominal region. J Emerg Tradit Chin Med (Chin) 2007;16:1238-1240.
23. Song D, Wang ZT, Li LY, Zhong GY. Protective effect of lobetyolin on gastric mucosa of experimental gastric ulcer in rats. J Emerg Tradit Chin Med (Chin) 2008;17:963-964.
24. Chan LW, Cheah EL, Saw CL. Antimicrobial and antioxidant activities of *Cortex Magnoliae Officinalis* and some other medicinal plants commonly used in south-east Asia. Chin Med 2008;28:3-15.
25. Liu CB, Zhang SC, Li QT. The development of modern pharmacological research of rhizoma cyperi. Guangming J Chin Med (Chin) 2009;24:787-788.

(Received July 12, 2012)
Edited by ZHANG Wen