Effect of herbal formula Xiao Pi-II on functional dyspepsia

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Abstract

OBJECTIVE: To investigate the therapeutic effect of the herbal medication Xiao Pi-II on the symptoms and gastric motility of patients with functional dyspepsia (FD).

METHODS: A total of 180 FD patients were divided randomly and equally into Xiao Pi-II and mosapride groups. The two groups were treated with Xiao Pi-II (100 mL, t.d.s., ante cibum) and mosapride (5 mg, t.d.s., ante cibum) for 2 weeks. Before treatment and 3 days after all medication was stopped, patients responded to a questionnaire evaluating gastrointestinal symptoms and were assessed with abdominal three dimensional ultrasonography (3D-US) for gastric motility.

RESULTS: Gastrointestinal symptoms (especially bloating, post-prandial fullness and eructation) were improved significantly in FD patients treated with Xiao Pi-II (P<0.05, P<0.05, and P<0.05), but no significant difference was found in the mosapride group (P>0.05). The effective rates in the Xiao Pi-II and mosapride group were 86.7% and 60.0%, respectively (P<0.05). The gastric liquid emptying rate (GLER) in the Xiao Pi-II group showed a significant increase (P<0.01) after 2 weeks of treatment but there was no significant change (P>0.05) of GLER in the mosapride group.

CONCLUSION: Compared with mosapride, Xiao Pi-II improved symptoms and GLER significantly in FD patients with delayed gastric emptying.

INTRODUCTION

Functional dyspepsia (FD) is characterized by unexplained post-prandial fullness, early satiety and epigastric pain or burning. An epidemiological survey in Western countries showed that the prevalence of FD ranged from 11.5% to 14.7%. FD is a common problem in outpatients and tends to be a chronic condition. Some long-term studies demonstrated that symptoms persisted in >80% of affected patients after 6-7 years of follow-up, which reduced patients’ quality of life (QoL) and increased the economic burden of medical care.

FD is diagnosed if no structural or biochemical explanations for the symptoms can be identified after appropriate investigations. The etiology and pathophysiology of FD remains unclear, but several factors have been proposed: altered visceral sensitivity and perception; gastrointestinal motor and secretion dysfunction; infection by Helicobacter pylori; and psychosocial factors. Delayed gastric emptying was initially considered to be the main cause of symptoms in patients with FD because it was reported to occur in a subset of patients with FD, ranging from 25% to 50%. It is assumed that delayed gastric emptying and consequent prolonged antral distension can reduce hunger, increase satiety, and cause symptoms such as early satiety and post-prandial fullness.
tiety, and even cause gastric discomfort, all of which would pose an appreciable barrier to adequate nutrition. Delayed gastric emptying may influence the function of gastrointestinal secretion, which in turn may further affect gastrointestinal motility, resulting in alterations in the luminal chemical environment, abnormal duodenum gastric bile reflux, and FD symptoms. Accordingly, delayed gastric emptying is a focal point of debate about anorexia caused by dyspepsia, and prokinetic agents are often administered for its treatment in Japan. Recently, it was reported that post-prandial fullness was the most severe symptom in patients who reported aggravation of their symptoms by consuming a meal. Standard pharmacological treatment includes anti-secretory agents and prokinetics, but these are often unsatisfactory, leading to the use of largely unproven alternatives. Dissatisfied patients are likely to search for alternative medication elsewhere if conventional therapies fail. This is often the case with patients suffering from functional gastrointestinal disorders (FGID) because the treatment options have limited efficacy.

Based on the Traditional Chinese Medicine (TCM) theory of "reinforcing spleen Qi," Xiao Pi-II is prepared with nine Chinese herbs: Dangshen (Radix Codonopsis), Baizhu (Rhizoma Atractylodis Macrocephalae), Cangzhu (Rhizoma Atractylodis Lanceae), Fuling (Poria), Banxia (Rhizoma Pinelliae), Shaten (Fructus Amomi), Zhiqiao (Fructus Aurantii Submatutus), Gancao (Radix Glycyrrhizae), and Zhiqiao (Zizyphus franklinii), used to regulate gastrointestinal motility and treat FD. In the present study, we compared Xiao Pi-II with mosapride for the treatment of FD by assessing symptomatic improvement, including the rate of emptying of gastric liquids.

MATERIALS AND METHODS

Subjects

Patients with FD were recruited from the clinic of the Gastroenterology Department of the First Affiliated Hospital of Liaoning Medical University. A total of 180 patients meeting the diagnostic criteria described below were divided randomly into Xiao Pi-II group and mosapride group for a single-blind clinical study. The Xiao Pi-II group comprised 90 patients (47 males; average age, 42 ± 15 years; range, 21-63 years). The mosapride group comprised 90 subjects (49 females; average age, 43 ± 14 years; range, 23-58 years). The study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Liaoning Medical University (Jinzhou, China). All participants provided written informed consent to be involved in the study.

Inclusion criteria

According to the Rome III Diagnostic Criteria for Functional Gastrointestinal Disorders, FD can be diagnosed by (a) meal-induced dyspeptic symptoms and post-prandial distress syndrome (PDS) and (b) epigastric pain. Patients diagnosed with PDS were included in this study.

The diagnostic criteria of PDS are duration of ≥3 months with onset ≥6 months previously with one or both of the following symptoms: (a) bothersome post-prandial fullness occurring after ordinary sized meals at least several times a week; and (b) early satiation that prevents completion of a regular meal at least several times per week. The support criteria are: (a) upper abdominal bloating, post-prandial nausea or excessive belching can be present; and (b) PSD may coexist with epigastric pain syndrome (EPS).

All participants underwent endogastroduodenoscopy (EGD) before enrollment. They were examined by gastroenterologists to determine if the EGD observations were related to current dyspeptic symptoms.

Exclusion criteria

Patients having any one of the following conditions were excluded: history of peptic ulcers; gastroesophageal reflux disease (GERD); mental disorders; aggravating malignant tumors or other serious consumptive disease; susceptibility to infection and bleeding; serious conditions in the cardiovascular, hepatic, renal, gastrointestinal or hematological systems. They were also excluded if they: had contraindications to mosapride; were unconscious; had previously undergone gastrointestinal surgery; were pregnant or lactating.

At the screening phase, patients who were using any antibiotic, proton-pump inhibitor, bismuth salt, prokinetic agent (e.g., itopride) or herbal medication, or who were participating in any other clinical trial, were excluded.

Assessment of symptoms

Symptoms were assessed according to the Stanghellini criteria: 0=absent; 1=occasionally present but not affecting daily activities; 2=present moderately often, slightly affecting activities; and 3=present moderately or more often, affecting activities considerably. The symptom complex index (SCI) was calculated by dividing the summation of all the scores of the presenting symptoms by the number of symptoms.

Assessment of efficacy

Efficacy was assessed using the following scale: "noticeable efficiency" was if the SCI was less than the pretreatment value by ≥2; "efficiency" was if the SCI was less than the pretreatment value by ≥1 but <2; and "inefficiency" was if the SCI was less than the pretreatment value by <1.

Dropouts

Dropout cases included those who: had poor compliance; were subjected to severe adverse events; had complications or with special physical changes that meant that they could not continue the trial; quit the trial by themselves.
**Table 1 Comparison of the symptom scores before and after treatment for the two groups (̅ ± s)**

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>Epigastic pain</th>
<th>Bloating</th>
<th>Postprandial fullness</th>
<th>Eructation</th>
<th>Nausea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xiao Pi-II</td>
<td>90</td>
<td>Pre-treatment</td>
<td>1.62±0.48</td>
<td>2.62±0.61</td>
<td>2.32±0.57</td>
<td>2.12±0.69</td>
<td>1.76±0.46</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post-treatment</td>
<td>1.58±0.67</td>
<td>1.16±0.32*</td>
<td>1.28±0.68*</td>
<td>1.33±0.36*</td>
<td>1.68±0.67</td>
</tr>
<tr>
<td>Mosapride</td>
<td>90</td>
<td>Pre-treatment</td>
<td>1.75±0.24</td>
<td>2.63±0.42</td>
<td>2.61±0.43</td>
<td>2.44±0.77</td>
<td>1.47±0.26</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post-treatment</td>
<td>1.83±0.52</td>
<td>2.34±0.56</td>
<td>2.53±0.25</td>
<td>2.67±0.30</td>
<td>1.56±0.52</td>
</tr>
</tbody>
</table>

Notes: *P<0.05, compared with the pre-treatment in the same group; †P<0.05, compared with the Xiao Pi-II group post-treatment.

**Table 2 Comparison of effective rates**

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Curative effect [n (%)]</th>
<th>Total effective rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Markedly effective</td>
<td>Effective</td>
</tr>
<tr>
<td>Xiao Pi-II</td>
<td>90</td>
<td>36 (40.0)</td>
<td>42 (46.7)</td>
</tr>
<tr>
<td>Mosapride</td>
<td>90</td>
<td>24 (26.7)</td>
<td>30 (33.3)</td>
</tr>
</tbody>
</table>

Notes: *P<0.05, compared with the mosapride group.
**Comparison of GLER**

Table 3 shows the comparison of the GLER between the two groups. The GLER in the Xiao Pi-II group was increased significantly (P<0.01) after 2 weeks of treatment. In contrast, there was no significant change (P>0.05) in the mosapride group (Table 3).

**Table 3 Comparison of gastric liquid emptying rate between before and after treatment**

<table>
<thead>
<tr>
<th>Before treatment (%)</th>
<th>After treatment (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GER of Xiao Pi-II</td>
<td>48±7</td>
<td></td>
</tr>
<tr>
<td>GER of mosapride</td>
<td>56±10</td>
<td>0.000*</td>
</tr>
</tbody>
</table>

Notes: GER: gastroesophageal reflux. *P<0.01, after treatment vs before treatment.

**DISCUSSION**

We found that Xiao Pi-II could increase GLER and improve gastrointestinal symptoms in PDS; Xiao Pi-II was superior to mosapride. The optimal treatment of PDS has not been established, but empirical pharmacological interventions with prokinetic agents have been shown to be effective in a subgroup of FD patients. Prokinetic" refers to a diverse group of medications that share the common characteristic of accelerating gastrointestinal motility. Evidence has suggested that the 5-HT4, (5-hydroxytryptamine 4) receptor-prefering agonist mosapride is a more promising prokinetic that stimulates the release of acetylcholine by exciting the 5-HT4 receptor of the myenteric nerve plexus, and strengthens the movement of the stomach and duodenum. The gastric emptying time (GET) in the mosapride group was reduced and indicated the obvious effect of mosapride on shortening the GET. Prokinetic agents clearly accelerate gastric emptying, but they often have little effect on (and sometimes can worsen) symptoms, particularly at higher doses.

Herbal medicines have a long history in the treatment of dyspeptic condition. A single herb or a combination of herbs is usually employed. The symptomatology of PDS is very similar to that of "Pi Man" (a name of a disease in TCM with bloating as the chief complaint). Deficiency of the spleen and stomach is the major cause of PDS. Xiao Pi-II showed significant effects on improving the symptoms of PDS, mainly owing to its effect of invigorating the spleen and replenishing Qi. In terms of TCM theory, the spleen and stomach function as one. They have vital roles in the metabolism of digestion and nutrition, and affect the functions of the immune, hematopoietic and muscular systems. Weakness of spleen and stomach result in hypofunction of digestion, absorption and metabolism. This leads to a decrease in internal nutrients and failure of general functional activities, disturbance of the immune system and, eventually, organic degeneration. Taking care of the spleen and stomach is important for body strengthening as well as the prevention and treatment of diseases.

The main ingredient of Xiao Pi-II, Danshen (Radix Codonopsis), has regulatory actions on gastrointestinal motility, influences basic electrical rhythms in the gastrointestinal tract, and reduces the increasing action of gastric motility and emptying upon stress in rats. Fuling (Poria) Cocos possesses inhibitory effects on mucosal-type mast cells, which may (at least in part) explain the therapeutic effect on functional gastrointestinal disorders. Cangzhu (Rhizoma Ararctylobis Lanceae), Sharen (Fructus Amomi), and Banxia (Rhizoma Pinelliae) can accelerate delayed gastric emptying in rats. In conclusion, Xiao Pi-II can improve gastric emptying and the gastrointestinal symptoms of patients with FD. The findings lend further evidence to the potential of Xiao Pi-II as a new option for the treatment of FD.

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