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ORIGINAL ARTICLE

Electroacupuncture Accelerates Solid Gastric Emptying and Improves Dyspeptic Symptoms in Patients with Functional Dyspepsia

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Abstract The aims of this study were to investigate the effects of electroacupuncture (EA) at ST36 and PC6 points on solid gastric emptying and dyspeptic symptoms in patients with functional dyspepsia. Nineteen patients with functional dyspepsia (FD) were involved in the study, consisting of two parts: (1) acute effects of EA on solid gastric emptying in FD patients with delayed gastric emptying and (2) short-term (2-week) effects of EA on symptoms in FD patients with normal gastric emptying. Results were as follows. (1) Ten of the19 patients showed delayed gastric emptying of solids, and acute EA significantly improved delayed gastric emptying; the halftime for gastric emptying was reduced from 150.3 ± 48.4 to 118.9 ± 29.6 min ($P = 0.007$). (2) In the nine patients with normal gastric emptying, 2-week EA significantly decreased the symptom score, from 8.2 ± 3.3 at baseline to 1.6 ± 1.1 ($P < 0.001$) at the end of treatment. We conclude that EA at the ST36 and PC6 points accelerates solid gastric emptying in FD patients with delayed gastric emptying and relieves dyspeptic symptoms in FD patients with normal gastric emptying.

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Introduction

Functional dyspepsia is a common clinical disease in the general population. Patients with functional dyspepsia often complain of a series of symptoms such as abdominal pain, bloating, nausea, and vomiting, which severely affect their quality of life. Among the patients with functional dyspepsia, delayed gastric emptying was observed in about 35% of patients [1, 2]. How to improve delayed gastric emptying and relieve dyspeptic symptoms in patients with functional dyspepsia is a challenge to gastroenterologists.

Although various therapeutic approaches have been reported, the outcome of the treatment for functional dyspepsia is poor. Social and economic costs for functional dyspepsia are enormous. In patients without risk factors, an empiric therapy with prokinetic agents (e.g., metoclopramide), acid suppressants (histamine-H2 receptor antagonist), and/or antimicrobial agents with activity against *Helicobacter pylori* are usually considered [3, 4]. Irrespective of morbid anxiety or depression, psychotropic agents are occasionally applied in refractory patients with functional dyspepsia. Treatment of functional dyspepsia is a challenge to clinical doctors because there is a need to balance medical management strategies and treatments for psychologic or functional diseases. Conventional therapies for these patients are still unsatisfactory. There are a fair number of patients who are refractory to medical therapies and the side effects also limit the application of the therapies.

Acupuncture, an ancient Chinese traditional method, has been shown to be effective in the treatment of various functional diseases and the normalization of abnormal

physiological conditions in humans. Acupuncture has been shown to improve nausea and vomiting in various clinical settings, such as in patients with postsurgery and chemotherapy, and to be effective in the treatment of addiction, stroke rehabilitation, headache, menstrual cramps, tennis elbow, fibromyalagial pain, osteoarthritis, low back pain, and carpal tunnel syndrome [5, 6]. Effects of acupuncture on the digestive system have also been investigated recently. Acupuncture was reported to decrease gastric acid output and serum gastrin concentration and enhance the gastric mucosal barrier [7–14]. More than one acupuncture point is commonly used for the treatment of gastrointestinal functional disorders. Electroacupuncture (EA) at the PC6 (Nanguan) and ST36 (Zushanli) acupoints accelerated gastric emptying of liquid in a canine model [15] and improved gastric dysrhythmia in healthy volunteers; EA at ST36 improved gastric emptying of liquid in rats [16]. However, little is known about the therapeutic potential of EA for functional dyspepsia.

Therefore, the aims of this study were to investigate the effects of electroacupuncture at the ST36 and PC6 points on solid gastric emptying and dyspeptic symptoms in patients with functional dyspepsia.

Materials and methods

Subjects

The study was performed in 19 outpatients with functional dyspepsia (5 men, 14 women; age, 22 to 58 years; mean, 43 years) and 12 healthy volunteers without any gastrointestinal symptoms (6 men, 6 women; age, 21 to 56 years; mean, 42 years). All subjects were diagnosed of functional dyspepsia according to the Rome II criteria [17]. The patients had dyspeptic symptoms, including nausea, abdominal distension, early satiety, belching, and abdominal pain, and the symptoms had lasted for more than 3 months in the past year. Twelve age- and sex-matched healthy controls were also included in the study to establish parameters of normal gastric emptying. Physical examination was performed in these healthy controls to rule out any systemic diseases and history of any gastrointestinal surgeries. This study was approved by the Ethics Committee of Union Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China. Written consent was obtained from each subject before the study.

Study protocol

The study was composed of two parts: an acute study to investigate the effect of EA on gastric emptying and a short-term study to investigate the effect of EA on dyspeptic symptoms.

The acute study consisted of two sessions on 2 separate days (session 1, sham stimulation; and session 2, real stimulation). In session 1, all 19 subjects received sham EA (electrical stimulation was performed via needles inserted at points that were 2 cm away from point ST36 or PC6). Only the patients with delayed gastric emptying from session 1 participated in session 2, in which real EA at PC6 and ST36 was performed. Sham or real EA was performed for 30 min before and 30 min after a standard test meal. The patients were blinded for sham or real EA, and so was the technician who assessed gastric emptying. Gastric emptying was monitored for a period of 4 hr. The classification of patients with delayed or normal gastric emptying was based on the mean half-time gastric emptying in healthy controls. Patients with a half-time gastric emptying greater than the mean ± SD of the half-time gastric emptying in healthy controls were classified as delayed gastric emptying. Otherwise, they were classified as normal gastric emptying. This specific definition (mean ± SD) was used so that the patients could be almost equally divided into two groups.

The short-term study was performed only in patients with normal gastric emptying. EA at PC6 and ST36 was performed twice a week for a period of 2 weeks. Dyspeptic symptoms were graded and scored at baseline, at the end of the first treatment session, and at the end of the 2-week treatment to assess the acute and short-term effects of EA, respectively. The symptoms, including nausea, early satiety, distension, abdominal pain, and belching, were graded from 0 to 3 as follows: 0, no symptom; 1, the symptom existed but could be ignored if the patient was not reminded of it; 2, the symptom persisted and could not be ignored; 3, the symptom persisted and affected daily life.

Electroacupuncture

Acupuncture points ST36 and PC6 were chosen since they were previously shown to accelerate gastric emptying of liquid in dogs [15]. PC6 is located in the groove caudal to the flexor carpi radialis and cranial to the superficial digital flexor muscles, 3 cm proximal to the corpus. ST36 is located at the proximal one-fifth of the craniolateral surface of the leg distal to the head of the tibia in a depression between the muscles of the cranial tibia and the long digital extensor. Two-channel electrical stimulation was performed via four stainless-steel acupuncture needles (0.3 × 5 mm) inserted into these four acupoints using a pulse generator (model G6805-2A; Shanghai Huayi Medical Instrument Factory, Shanghai, China). The electrical stimuli consisted of pulse trains with a train-on time of 2 sec and a train-off time of 3 sec. The pulses in each train were of a frequency of 25 Hz and an amplitude of 4 mA. The acupuncture needles were inserted to the appropriate depth by manual stimulation (slight thrusting, slight withdrawal, or twirling),

with the subject feeling some aching pain or numbness or warmth.

Gastric emptying

Scintigraphic scanning was used to measure the gastric emptying of solids. A low-fat meal [18] of 255 kcal was used in the measurement of solid gastric emptying, including 120 g scrambled egg (60 kcal), two slices of bread (120 kcal), 30 g strawberry jam (75 kcal), and 120 ml water; 1 mCi of ^{99}Tc-labeled sulfur colloid was mixed with the egg substitute as the meal marker; then this mixture was cooked in a microwave for 2 min, with stirring. The meal was prepared just before the initation of the study and taken by all subjects within 10 min. Scintigraphic scanning was taken at 0, 30, 60, 120, and 240 min after the meal. The region of interest was drawn around the stomach on the anterior and posterior images for each frame during the scanning time.

Statistical analysis

All data are expressed as means ± SD. Analysis of variance (ANOVA) was used to test the difference among three or more groups. Student's *t*-test with Bonferroni correction was applied to compare the paired data. A value of $P < 0.05$ was considered statistically significant.

Results

Gastric emptying in functional dyspepsia

The mean half-time of solid gastric emptying was 106.2 ± 7.0 min in the 12 healthy volunteers; therefore a patient with a half-time of gastric emptying greater than 114 min (mean ± SD) was classified into the delayed gastric emptying group. Based on this definition, 52.6% (or 10/19) of the functional dyspeptic patients were classified into the group of delayed gastric emptying, with a half-time of gastric emptying of 150.3 ± 48.4 min ($P < 0.05$ vs. healthy controls), and 47.4% (or 9/19) were classified into the group of normal gastric emptying, with a half-time of gastric emptying of 99.9 ± 14.6 min ($P > 0.05$ vs. healthy controls).

Effects of electroacupuncture on gastric emptying

EA normalized gastric emptying in patients with delayed gastric emptying; the half-time of gastric emptying in the real stimulation session was 118.9 ± 29.6 min, which was significantly shorter than that in the sham stimulation session ($P = 0.007$; Fig. 1) and comparable with that in the healthy volunteers ($P > 0.05$). Comparisons between the real and the sham EA sessions at different postprandial points are listed in Table 1. A significant acceleration in gastric emptying was seen with EA at all points except for 4 hr after the meal.

Table 1 Gastric emptying (GE)

Case	% of GE			
	30 min	60 min	120 min	240 min
Sham	10.9 ± 2.8	21.1 ± 5.2	42.7 ± 9.3	88.4 ± 18.0
Real	13.1 ± 3.4	25.4 ± 7.4	51.4 ± 11.9	96.0 ± 8.4
Control, 12	15.4 ± 1.7	30 ± 3.4	60.8 ± 6.2	100.0 ± 0.0
F	5.55	5.83	7.37	2.63
P	0.01	0.008	0.003	0.09

Note. *P* values are for differences among the three groups calculated by ANOVA.

Effects of electroacupuncture on dyspeptic symptoms

Both acute and short-term EA improved dyspeptic symptoms in functional dyspeptic patients with normal gastric emptying (see Fig. 2). The mean total symptom score was 8.22 ± 3.27 at baseline and decreased significantly, to 3.77 ± 1.98 ($P < 0.05$), at the end of the first EA session and further reduced to 1.56 ± 1.13 at the end of the 2-week EA treatment ($P < 0.001$ vs. baseline, $P < 0.05$. vs. the first session).

The mean scores of the individual symptoms were all significantly decreased after the first EA session and the 2-week EA therapy compared with the baseline ($P < 0.05$) (see Fig. 3). Similarly, the individual symptom score was significantly lower after the 2-week EA therapy than after the first EA session ($P < 0.05$) (see Fig. 4).

No difference in symptom score was noted at baseline between patients with delayed gastric emptying and patients with normal gastric emptying. Acute EA also resulted in a significant decrease in symptoms in patients with delayed

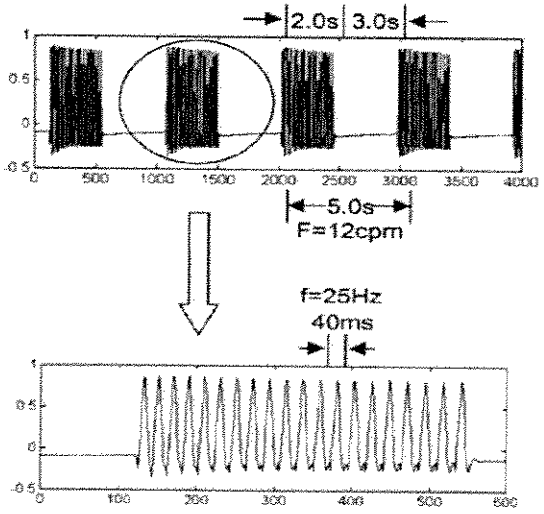

Fig. 1 Stimulus of electroacupuncture

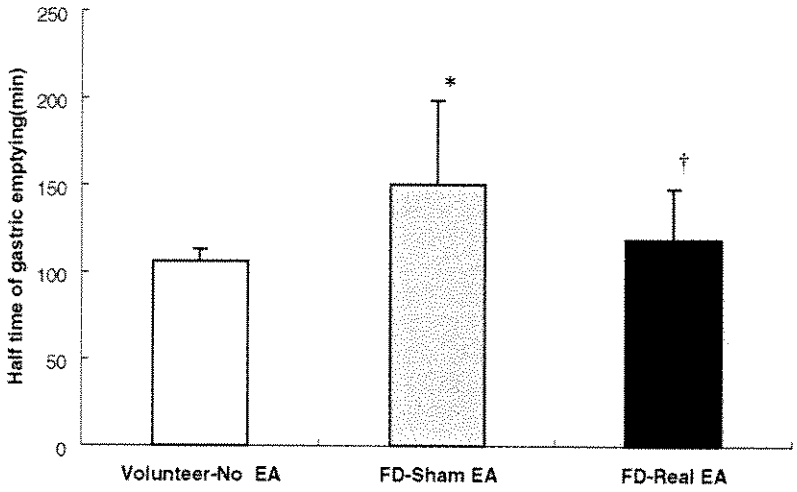

Fig. 2 Gastric emptying half-time in healthy volunteers and functional dyspepsia patients with sham EA and real EA.*$P < 0.05$ vs. volunteers without EA.†$P < 0.05$ vs. sham EA by paired Student's *t*-test

gastric emptying (baseline of 7.68 ± 2.2 vs. acute EA of 2.76 ± 1.58; $P < 0.05$).

Discussion

In this study, we found that EA accelerated and normalized gastric emptying in functional dyspeptic patients with delayed gastric emptying. Acute EA improved dyspeptic symptoms in both groups of patients, with normal and delayed gastric emptying. A short-term treatment of 2 weeks resulted in further improvement in the symptoms in patients with normal gastric emptying.

EA instead of manual acupuncture was performed in this study because EA is reproducible, whereas the outcome of manual acupuncture is directly related to the acupuncturist and therefore not necessarily reproducible. EA was not applied in patients with normal gastric emptying or control subjects because there was not much room for improvement with EA since gastric emptying was already normal in these subjects. It should also be noted that the definition of delayed gastric emptying in this study was the mean minus one instead of two standard derivations. This was used to classify patients with almost-equal numbers of "normal" gastric emptying and "delayed" gastric emptying. This was the definition for this particular study and not for any clinical purposes.

The PC6 and ST36 acupoints were chosen as the stimulation points in the present study. Among many acupuncture points, PC6 and ST36 have frequently been chosen to treat disorders related to the gastrointestinal tract [5–13, 15, 16, 19–27]. Some previous studies reported that stimulation at these two acupuncture points exerted good effects on the digestive system [7–13, 15, 16, 19–27], including normalizing the dysrhythmia of EGG and improving gastric emptying [15, 23, 28]. Electrical stimulation with pulse trains was widely applied in clinical settings for acupuncture treatment.

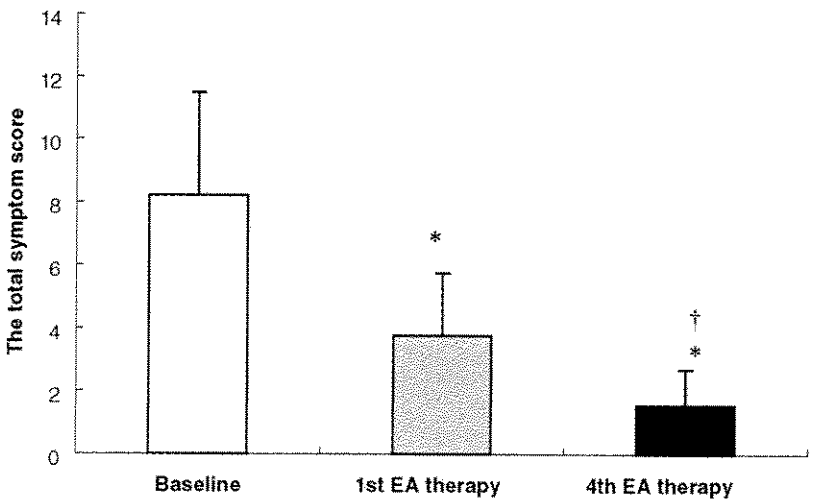

Fig. 3 Total symptom score in patients with normal gastric emptying at baseline and immediately after the first real EA therapy and fourth real EA therapy. The total symptoms score immediately after the first and fourth real EA therapies were both significantly lower than that at baseline (ANOVA, $P < 0.001$; paired *t*-test, $P < 0.05$). The total symptoms score after the fourth EA was significantly lower than that after the first EA ($P < 0.05$).*$P < 0.05$ vs. baseline by nonparametric test. †$P < 0.05$ vs. first real EA therapy by nonparametric test

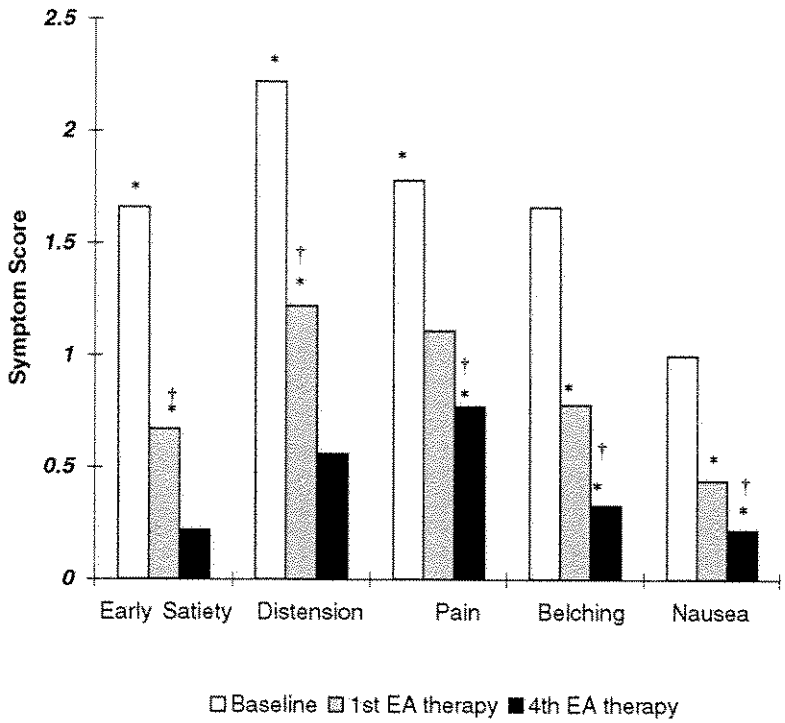

Fig. 4 Individual symptom score in patients with normal gastric emptying at baseline and immediately after the first and fourth real EA therapies. All individual symptom scores immediately after the first and fourth real EA therapies were significantly lower than that at baseline (ANOVA, $P < 0.001$; paired t-test, $P < 0.05$). The individual symptom score after the fourth EA therapy was also significantly lower than that after the first EA therapy ($P < 0.05$). $^*P < 0.05$ vs. baseline by nonparametric test. $^\dagger P < 0.05$ vs. first real EA therapy by nonparametric test

In this study, we found that EA at the PC6 and ST36 points significantly accelerated solid gastric emptying. Although acupuncture has been widely practiced in some countries and numerous research papers on acupuncture are available, its effect on gastric emptying or motility is still not fully understood. While there have been some animal studies investigating the effect of acupuncture on gastric emptying and motility [15, 23–27], according to our knowledge, the present study is the first to investigate the effect of acupuncture on gastric emptying in human subjects.

The mechanism of acupuncture in the improvement of gastric motility and symptoms is still unknown. Gastric motility is regulated by a number of factors. It has been reported that EA at both the PC6 and the ST36 points can reduce arrhythmia and normalize gastric slow waves [28]. EA at the ST36 point alone reduced tachygastria in patients with diabetic gastroparesis [29, 30]. Tatewaki et al. [26] confirmed that EA had dual effects, either stimulatory or inhibitory. It had an excitatory effect when gastric, pyloric and intestinal motility is of hypomotility or inhibitory effect in the case of hypermotility. Most previous studies investigated the effects of acupuncture on liquid gastric emptying in animals and the possible mechanism was attributed to exciting vagal activity [15] and enhancing gastric myoelectrical activity [8, 28].

The results of this study suggest that acupuncture is able to relieve dyspeptic symptoms in patients with functional dyspepsia. The total symptom score was reduced and each symptom was improved. These symptoms are common in patients with functional dyspepsia and gastroparesis. Prokinetic agents have been widely used for the treatment of dyspeptic symptoms, but with limited effects. It is a common and traditional belief in Chinese Traditional Medicine that acupuncture is useful to reduce various symptoms, especially chronic pain. However, there is limited scientific evidence to confirm this. Recently, results from a number of randomized controlled trials have provided convincing evidence of the efficacy of acupuncture in treating nausea and vomiting in adult patients associated with various conditions, such as postsurgery, hemotherapy, pregnancy, and motion sickness [5]. Acupuncture has also been applied in animal models of vomiting in a few studies. The number of emetic episodes induced by morphine [19] or cyclophosphamide [20] was significantly reduced by electrical acupuncture at the PC6 point in ferrets. In dogs, electrical acupuncture at both the PC6 and the ST36 points reduced the incidence of vomiting and symptomatic behaviors, suggesting nausea induced by vasopressin [32]. In that particular study, a similar improvement in emetic symptoms was also observed with gastric electrical stimulation. It was reported that the improvement with both EA and gastric electrical stimulation was mediated via the vagal pathway, as no improvement was noted in the dogs with vagotomy. The exact mechanisms involved in this current study were not clear. However, except for several case reports on the treatment of functional dyspepsia with acupuncture, few data are available on the effect of acupuncture on dyspeptic symptoms. In one study with 103

patients, acupuncture was reported to be effective in reducing dyspeptic symptoms (mainly epigastric pain) in 95% of them [33]. However, no detailed information on the main dyspeptic symptoms (nausea, early satiety, distension, abdominal pain, and belching) after acupuncture therapy was described. Relief of dyspeptic symptoms with EA in patients with functional dyspepsia in the current study suggests the potential of EA for the treatment of symptomatology in patients with functional dyspepsia.

In conclusion, EA at the ST36 and PC6 points significantly accelerates solid gastric emptying and improves dyspeptic symptoms in patients with functional dyspepsia. EA may be a potential therapy for treatment of functional dyspepsia.

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