Electroacupuncture accelerates gastric emptying in association with changes in vagal activity

HUI OUYANG, JIEYUN YIN, ZHISHUN WANG, PANKAJ J PASRICH, J. D. Z. CHEN
Division of Gastroenterology, University of Texas Medical Branch, Galveston, Texas 77555-0632

Received 20 June 2001; accepted in final form 26 October 2001

Ouyang, Hui, Jielyn Yin, Zhishun Wang, Pankaj J Pasricha, J. D. Z. Chen. Electroacupuncture accelerates gastric emptying in association with changes in vagal activity. Am J Physiol Gastrointest Liver Physiol 282: G390–G396, 2002; 10.1152/ajpgi.00272.2001.—Gastroparesis is a disorder with a lack of treatment options and this study investigated the effect of electroacupuncture on gastric emptying and involved mechanisms. Dogs implanted with a duodenal cannula and serosal electrodes were fed with Ensure mixed with phenol red, and the gastric effluent was collected. Electroacupuncture was performed from 30 min before until 45 min after the meal. Gastric myoelectrical activity and electrocardiogram were recorded. Gastric emptying was significantly improved with electroacupuncture. Vaginal activity assessed from the spectral analysis of heart rate variability was markedly increased with electroacupuncture. Electroacupuncture increased the regularity of gastric slow waves in both the proximal and distal stomach. It also increased the number of spike bursts in the distal but not proximal stomach. Electroacupuncture accelerates gastric emptying of liquid in dogs and its potential for treating gastroparesis may be explored. The effect may be attributed to improvement in gastric slow-wave rhythmicity and antral contractile (spike) activity and may possibly involve the vagal pathway.

Gastroparesis; gastric myoelectrical activity; heart rate variability

Electroacupuncture has been used empirically in clinical practice in oriental countries for several millennia and is being increasingly accepted by practitioners and patients in the West as well (4, 25). Electroacupuncture is a modification of this technique that stimulates acupuncture points with electrical current instead of manual manipulations, and appears to have more consistently reproducible results in both clinical and research settings (17, 21, 40). Both conventional and electrical acupuncture have been used for a variety of ailments, particularly for the relief of pain (10, 16, 31). Recently, an National Institutes of Health consensus statement was published (25), confirming the promising therapeutic effects of acupuncture for the treatments of postoperative dental pain, and postoperative and chemotherapy nausea and vomiting. Recent studies (9, 12, 14, 30, 32, 33, 38) have begun exploring the effects of acupuncture on gastrointestinal physiology and its potential for the treatment of gastrointestinal diseases. However, despite its well-known effects on nausea and vomiting, relatively little attention has been paid to its potential for the management of disorders of gastrointestinal motility (19, 27). Such disorders include gastroparesis, defined as delayed gastric emptying, for which there are few, if any, effective forms of conventional therapy. We hypothesized that electroacupuncture could accelerate gastric emptying, and we tested this hypothesis in a canine model previously validated in our laboratory.

METHODS

Experimental Design

Effects of electroacupuncture on gastric emptying of liquid and gastric myoelectrical activity were assessed in female hound dogs that had undergone preparation with duodenal cannulation and placement of gastric serosal electrodes during a prior laparotomy (see Animals and Surgical Preparation). There were two sessions, one control session without electroacupuncture and the other with electroacupuncture to study the effect of electroacupuncture on gastric emptying of liquid. In a separate experiment, the effect of electroacupuncture on heart rate variability, a measure of vagal tone, was studied. This experiment was performed in the fasting state to avoid compounding effects of meal ingestion on heart rate variability.

Animals and Surgical Preparation

The study was performed in seven healthy female hound dogs (13–20 kg). After an overnight fast, each dog was anesthetized with Pentothal (sodium thiopental 5 mg/kg, intravenous; Abbott Laboratories, N. Chicago, IL) and maintained on IsoFlo (isoflurane 1.5%, inhalation anesthesia; Abbott) in oxygen-nitrous oxide (1:1) carrier gases delivered from a ventilator after endotracheal intubation. Each dog was monitored with the assessment of tongue color, pulse rate, and breath rate. Eight pairs of 28-gauge cardiac pacing wires (A&E Medical, Farmingdale, NJ) were implanted on the gastric serosa along the greater curvature by laparotomy. The most distal pair was 2 cm above the pylorus, and the distance between adjacent pairs of electrodes was 2 cm. Two electrodes in each pair were about 0.5 cm apart. Electrodes were penetrated into the subserosal layer and were affixed to the gastric serosa by nonabsorbable sutures. Wires were
tunneled through the anterior abdominal wall subcutaneously along the right side of the trunk, and were placed outside the skin around the right hypochondrium for attachment to the recorder or the stimulator. A cannula was placed in the duodenum 20 cm beyond the pylorus for assessment of gastric emptying. The dogs were transferred to recovery cages after receiving medications for postoperative pain control. The study was initiated after the dogs were completely recovered from the surgery, usually 2 wk after the surgery. The dogs were in a conscious state during the study and were restrained and supported by a sling. The study was approved by the animal care and use committees of the Veterans Affairs Medical Center, Oklahoma City, OK, and of the University of Texas Medical Branch at Galveston, TX.

Measurement of Gastric Emptying

The study of gastric emptying consisted of two sessions, with or without electroacupuncture, in a randomized order. After an overnight fast, a baseline recording of gastric myoelectrical activity was made for a period of 30 min and then electroacupuncture was initiated. Thirty minutes later, a liquid meal of one can of Ensure (Ross Products Division Abbott Laboratories, Columbus, OH) mixed with 100 mg of phenol red was ingested. One can (237 ml) of Ensure contained 250 calories (6 g fat, 40 g carbohydrates, and 9 g protein). Forty-five minutes after the meal, electroacupuncture was terminated. Gastric myoelectrical activity and gastric emptying were monitored for another 45 min after the termination of electroacupuncture. Gastric effluent was collected via the cannula every 15 min during the entire 90-min postprandial period. A balloon was inserted into the small intestine through the cannula and inflated immediately after ingestion of the meal. The balloon was placed 5 cm distal to the cannula and inflated with 10 ml of air to block the distal flow of gastric effluent and to delay gastric emptying. Inflation of the balloon with 10 ml of air was determined by a previous study (18) in which vomiting was noted in some dogs with a balloon inflation of 30 ml of air. The protocol of the control session was the same except that electroacupuncture was not performed.

Measurement of Gastric Myoelectrical Activity

A multichannel recorder (model EOG 100A, Acqknowledge III; Biopac Systems, Santa Barbara, CA) was used to record gastric myoelectrical activity via the eight pairs of serosal electrodes during the entire study. All signals were displayed on a computer monitor and saved on the hard disk of an IBM-compatible 486 personal computer. The high cutoff frequency of the amplifier was 35 Hz with an initial sampling frequency of 100 Hz. For the spectral analysis of gastric slow waves, the signals were further filtered using a digital low-pass filter with a cutoff frequency of 1 Hz and down-sampled at 2 Hz to avoid the violation of the Nyquist theory. Custom-made computer software developed and validated in our laboratory (3) was applied to compute the percentage of normal 4–6 cycles per minute (cpm) gastric slow waves. In this method, the gastric myoelectrical recording was divided into blocks of 1 min each and the power spectrum of each 1-min recording was derived using the autoregressive moving average spectral analysis method. The minute of the recording was defined as normal if its power spectrum had a dominant peak in the frequency range of 4–6 cpm. Otherwise, it was defined as abnormal. The percentage of normal gastric slow waves was determined by the percentage of time during which a dominant spectral peak was noted in the frequency range of 4–6 cpm. The definition of the normal frequency range was based on analysis of our previous study (28) in the healthy dogs.

A special computer program validated in a previous study (36) was used to detect spikes from the gastric myoelectrical recording. The number of spike bursts per minute was calculated from the detected spikes.

To study a possible difference in gastric myoelectrical activity measured from the proximal stomach and the distal stomach, we have chosen to analyze the recordings from the most proximal two channels (representing the proximal stomach) and the most distal two channels (representing the distal stomach).

Measurement of Autonomic Function

The effect of electroacupuncture on autonomic function was assessed in a separate experiment performed on another day. The experiment was performed after an overnight fast and consisted of a 30-min baseline recording, a 30-min recording with electroacupuncture at PC6 (Neiguan) and ST36 (Zusanli) and a 30-min recovery period after the termination of electroacupuncture. An electrocardiogram (ECG) was recorded during the entire 90-min experiment from three cutaneous electrodes placed in the intercostal space below to the first pair of nipples (two active electrodes) and the right rear leg (one reference electrode) using a special one-channel amplifier with a cutoff frequency of 50 Hz (model 2283 FTI universal Fretrode amplifier; UFI, Morro Bay, CA). The recorded ECG signal was sampled at a frequency of 6,000 Hz using the analog/digital converter installed on the sound card of the computer. The digitized ECG was further down-sampled to 500 Hz. The heart rate variability signal was derived from the ECG recording using a special program developed in our laboratory (37) by identifying the R–R peaks, interpolating the R–R intervals so that the time interval between consecutive samples was equal and finally down-sampling the interpolated data to a frequency of 1 Hz.

Overall power spectral analysis was then applied to the heart rate variability signal and the percentage of power in each frequency subband was calculated. It was well known that the percentage of power in the low-frequency (LF) band (0.04 to 0.15 Hz) represents mainly sympathetic activity and the percentage of power in the high-frequency (HF) band (0.15 to 0.50 Hz) stands purely for parasympathetic or vagal activity. LF was computed as the ratio between the area under the curve in the frequency range of 0.04–0.15 Hz and the area under the curve in the frequency range of 0.04–0.50 Hz. Whereas, HF was assessed as the ratio between the area under the curve in the frequency range of 0.15–0.50 Hz and the area under the curve in the frequency range of 0.04–0.50 Hz. The ratio of LF/HF represents the sympathovagal balance.

Electroacupuncture Technique

Acupoints. Two acupuncture points used in this study were PC6 and ST36 (4, 35). 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. The location of ST36 is at the proximal one-fifth of craniolateral surface of the rear leg distal to the head of the tibia in a depression between the muscles of the cranial tibia and the long digital extensor. PC6 is a common acupuncture point used for the treatment of nausea and vomiting, whereas ST36 is one of the most frequently used acupuncture points for the treatment of gastric diseases. These two points were also used in our previous studies in both humans and dogs (19, 27).
Electrical stimulus. The electrical stimulus consisted of pulse trains (see Fig. 1). The frequency of the train was 12 cycles/min, and the duration of the train was 2 s. Pulses in each train had a frequency of 25 Hz and an amplitude of about 10 mA (model D-860; Shanghai Huayi Medical Instrument Factory, Shanghai, China).

Statistical Analysis
The paired Student’s t-test was applied to investigate the effects of electroacupuncture on the rate of gastric emptying, the regularity of gastric slow waves and gastric contractile activity between the electroacupuncture and control groups. ANOVA was used to compare the autonomic function data obtained during three different recording periods. Statistical significance was assigned for $P < 0.05$. All data were presented as means ± SE.

RESULTS
Effects of Electroacupuncture on Gastric Emptying
As shown in Fig. 2, the percentage of gastric retention was significantly less with electroacupuncture than that without electroacupuncture (at 15 min: $71.25 ± 5.97$ vs. $94.93 ± 3.50\%$, $P < 0.02$; at 45 min: $58.23 ± 5.60$ vs. $87.64 ± 4.40\%$, $P < 0.02$; and at 90 min: $49.12 ± 4.15$ vs. $70.85 ± 5.32\%$, $P < 0.04$). The difference in gastric retention between the sessions with and without electroacupuncture was $22.7\%$ at 15 min, $29.4\%$ at 45 min (a further reduction of $7\%$ in gastric retention with electroacupuncture), and $21.7\%$ at 90 min. It was noted that more emptying took place in the control session during the second 45-min post-prandial period (no stimulation was applied in this period in either session).

Effects on Gastric Myoelectrical Activity
In the control session without electroacupuncture, the proximal stomach showed a significantly higher percentage of regular 4–6 cpm slow waves ($91.1 ± 3.6$ vs. $79.5 ± 4.8\%$, $P < 0.01$), and a significantly higher number of spike bursts per minute ($3.8 ± 0.3$ vs. $1.5 ± 0.4$, $P < 0.0001$) than the distal stomach in the post-prandial state.

Electroacupuncture significantly increased the percentage of regular slow waves in the postprandial state in both the proximal ($97.5 ± 1.3$ vs. $91.1 ± 3.6\%$, $P < 0.03$) and distal stomach ($91.5 ± 2.4$ vs. $79.5 ± 4.8\%$, $P < 0.03$, see Fig. 3). Typical tracings showing gastric slow waves measured in the sessions with and without electroacupuncture are presented in Fig. 4. The dominant frequency of the postprandial gastric slow wave was, however, not affected by electroacupuncture in either the proximal ($5.32 ± 0.07$ vs. $5.30 ± 0.13$ cpm, $P = 0.2$) or distal ($5.27 ± 0.08$ vs. $5.33 ± 0.12$ cpm, $P = 0.3$) stomach.

Compared to the control session, electroacupuncture also increased the number of spike bursts per minute in the distal stomach ($2.0 ± 0.4$ vs. $1.5 ± 0.4$, $P < 0.04$)

Fig. 1. The electrical stimulus of electroacupuncture consisted of pulse trains. The frequency of the train was 12 cycles/min and the duration of the train was 2 s.

Fig. 2. Effect of electroacupuncture on gastric emptying. The percentage of gastric retention was significantly less with electroacupuncture than that without electroacupuncture. EA, electroacupuncture.

Fig. 3. Effect of electroacupuncture on gastric slow-wave rhythmicity. Compared with the control session, electroacupuncture significantly increased the percentage of the regular gastric slow waves in the postprandial state in both the proximal and distal stomach ($P < 0.03$).
but not in the proximal stomach (3.4 ± 0.4 vs. 3.8 ± 0.3, \( P = 0.2 \)).

**Effects of Electroacupuncture on Vagal Activity**

Spectral analysis of the heart rate variability signal revealed that electroacupuncture resulted in a significant enhancement of the vagal activity (ANOVA, \( P < 0.04 \)). The percentage of power in the HF band, which reflects vagal activity, was increased from the baseline value of 0.81 ± 0.01 to 0.85 ± 0.01 during electroacupuncture (\( P < 0.001 \)) and returned to a lower level during the recovery period after electroacupuncture (0.77 ± 0.03) (Fig. 5A). Similarly, the LF/HF ratio (representing the sympathovagal balance) was markedly changed during the three different periods of the experiment (baseline 0.23 ± 0.02 vs. electroacupuncture session 0.17 ± 0.01 vs. recovery period 0.33 ± 0.06, ANOVA, \( P < 0.04 \)) (Fig. 5B). Figure 6 presents an example of the increased HF in the power spectrum of the heart rate variability signal with electroacupuncture.

**DISCUSSION**

Although acupuncture or electroacupuncture has been widely practiced in some countries, and numerous research papers can be found in the literature, its effect on gastric emptying or motility is unknown. A previous canine study performed in our laboratory investigated the effect of electroacupuncture on gastric migrating motor complex. It was found that the duration of phase I of the migrating motor complex was decreased, whereas the length of phases II and III was increased (27). In the present study using a canine model, we have found that electroacupuncture at PC6 and ST36 significantly accelerated gastric emptying of liquid, improved gastric slow-wave rhythmicity and myoelectrical spike activity, and increased peripheral vagal activity.

Liquid gastric emptying is subject to several variables, the most important of which may be the tone of the proximal stomach. To understand the mechanism underlying the acceleration of gastric emptying in response to electroacupuncture, we monitored gastric myoelectrical activity in both the proximal and distal segments of the stomach. Control observations showed that the gastric slow wave had a homogeneous frequency in both the proximal and distal regions of the stomach and had higher amplitude in the distal stomach. This is in agreement with the general notion that the gastric slow wave propagates distally with increas-
An enhancement in gastric myoelectrical activity was observed with electroacupuncture, particularly in the distal stomach. Electroacupuncture completely abolished after vagotomy. Sato et al. (29) showed that when it was applied to a hindpaw, acupuncture-like stimulation elicited an excitatory gastric response. These authors proposed that acupuncture provoked a reflex that had cutaneous and muscle nerves as its afferent pathway, and the gastric vagus as its efferent pathway. Two previous studies (7, 15) reported an association between gastric dysrhythmias and so-called “sympathetic dominance.” Although accurate assessment of sympathetic activity was not available from the spectral analysis of the heart rate variability, the increase in parasympathetic activity with electroacupuncture observed in this study suggests a decrease in sympathetic activity or breakage of possible sympathetic dominance, leading to a reduction in gastric dysrhythmias or an increase in the percentage of normal slow waves.

Nausea and vomiting are relatively common symptoms that accompany a variety of gastrointestinal illnesses. They are the dominant symptomatology in gastroparesis or delayed gastric emptying, a disorder that may be idiopathic or secondary to diabetes, postsurgical states, or other acquired illnesses. Prokinetic agents have been used widely for the treatment of gastroparesis but with limited success (23, 24). More recently, there has been considerable excitement generated by the potential of gastric electrical pacing to improve symptoms in these patients. However, the largest trial on this subject did not show a significant improvement in gastric emptying (1). By contrast, little is known about the effects of acupuncture or electroacupuncture on gastric emptying in normal human subjects or patients. Hu et al. (13) examined the effects of electrical acustimulation at point PC6 on gastric slow waves and the severity of symptoms of motion

Autonomic function (6, 20), we performed an additional experiment in the fasting state on a separate day for the analysis of heart rate variability. A significant increase in vagal activity and a significant decrease in sympathetic activity were noted in association with electroacupuncture. Although we have no proof that this is responsible for the improvement in gastric emptying, it is certainly consistent with the hypothesis that the vagus may mediate some of the visceral effect of electroacupuncture, as suggested by earlier reports. Thus Xu (39) found that the regulatory effect of electroacupuncture on gastric dysrhythmia in rabbits was abolished after vagotomy.
Electroacupuncture accelerates gastric emptying

sickness as induced by a rotating drum. Electroacustimulation was reported to significantly reduce the severity of the symptoms of motion sickness and the associated tachygastria. In a previous study (19) performed in our laboratory, electroacupuncture with the same acupuncture points (PC6 and ST36) significantly increased the regularity of gastric slow waves in humans, measured from electrogastrography. In this current study, a significant increase in spikes (reflecting contractility) was noted in the distal stomach of dogs with the same technique. A substantial (more than twofold) increase in the rate of gastric emptying was noted during the 45-min postprandial period with electroacupuncture, an effect suggesting this method has real potential for the treatment of gastroparesis. The simplicity and noninvasive nature of this technique makes it a very attractive candidate therapy. We hope this study will stimulate future clinical studies needed to validate its use for this condition.

In summary, electroacupuncture at PC6 and ST36 substantially accelerates gastric emptying of liquid in dogs. Its clinical potential for the treatment of gastroparesis may be explored in future studies. The accelerating effect of electroacupuncture on gastric emptying may be attributed to the improvement in gastric slow-wave rhythmicity and antral contractile (spike) activity. Enhanced vagal activity with electroacupuncture suggests a possible involvement of vagal pathway in its regulation of gastric motility.

This study was partially supported by National Institute of Diabetes and Digestive and Kidney Diseases Research Grant 1R43-DK-55437-01.

REFERENCES


