

Effect of Electrical Stimulation on Acupuncture Points in Diabetic Patients with Gastric Dysrhythmia: A Pilot Study

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Key Words

Acupuncture · Diabetes mellitus · Gastric dysrhythmia

Abstract

Background/Aims: Abnormal gastric slow-wave frequencies have been observed in diabetic gastroparesis and are associated with impaired antral motor activity. In this study, we aimed at evaluating the effect of acupuncture on gastric slow waves in diabetic patients with symptoms suggesting gastric motor dysfunction. **Methods:** Fifteen patients with type II diabetes who had had dyspeptic symptoms for more than 3 months were enrolled. Two acupuncture needles were inserted into the subjects' legs at the Zusanli points, and electrical stimulation (2-Hz pulses) was delivered for 30 min. Cutaneous electrogastrography was performed for 30 min at baseline, for 30 min during acupuncture, and for an additional 30 min after acupuncture. Serum gastrin, motilin, and human pancreatic polypeptide levels were also measured. **Results:** There was a significant increase in the percentages of normal frequency during and after acupuncture (baseline vs. acupuncture and after acupuncture $21.99 \pm 19.38\%$ vs. 45.93 ± 19.72 and $48.92 \pm 19.56\%$; $p < 0.01$). In addition, the percentage of tachygastic frequency was decreased significantly during and after acupuncture. The dominant frequency was also

changed significantly. There was an increase of serum human pancreatic polypeptide during acupuncture (baseline vs. acupuncture 56.96 ± 27.64 vs. 73.11 ± 22.37 pmol/l; $p < 0.05$). **Conclusions:** The results of this study revealed that electrical stimulation at the Zusanli points could increase the percentage of normal electrogastrography frequency and decrease the percentage of tachygastic frequency in diabetic patients. The data indicate that acupuncture may enhance the regularity of gastric myoelectrical activity in diabetic patients.

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Introduction

Gastrointestinal (GI) dysmotility is a troublesome complication of diabetes mellitus that may be associated with significant morbidity from indigestion, nausea, vomiting, or dehydration [1]. Typical gastric motor and myoelectrical disturbances have been noted in patients with diabetic gastroparesis [2, 3]. The electrical pacemaker activity, known as the pacesetter potential or gastric slow wave [4], regulates the motor activity in the stomach. Abnormally high (tachygastic) or low (bradygastic) slow-wave frequencies have been observed in diabetic gastroparesis and are associated with impaired antral motor activity [5–7].

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Acupuncture has been used to treat GI symptoms in Oriental countries for many years. The most commonly used acupuncture points for treating GI symptoms are the Neiguan and Zusanli points [8]. Acupuncture at the Neiguan point in patients who underwent gynecological surgery had a significant antiemetic effect on postoperative nausea and vomiting [9], and it could also decrease cisplatin-associated nausea and vomiting in cancer patients [10]. Recently, electrical stimulation of the Neiguan point has been shown to enhance the regularity of gastric myoelectrical activity in healthy subjects [11]. However, there has been no report in the literature concerning the effect of acupuncture on gastric dysrhythmia in diabetic patients. Therefore, in this study, we aimed at evaluating the effect of acupuncture on the gastric slow wave in diabetic patients with symptoms suggesting gastric motor dysfunction. In addition, we monitored several GI peptides, including gastrin, motilin, and human pancreatic polypeptide (hPP), which are closely related to cholinergic regulation.

Patients and Methods

Patient Population

Fifteen patients with type II diabetes mellitus who had had dyspeptic symptoms for more than 3 months were included in this study. Symptoms included nausea, vomiting, upper abdominal discomfort, early satiety, bloating, and anorexia. There were 8 males and 7 females, age ranging from 42 to 77 (mean $\pm$ SD 63 ± 8.7) years. The duration of their diabetes mellitus ranged from 4 to 20 (mean 7.8) years. All patients showed evidence of autonomic neuropathy, as assessed by a standard series of cardiovascular reflex tests [12]. The serum HbA1C level before entering this study was $8.19 \pm 0.39\%$ (range 6.5 to 11.4%). An upper GI endoscopy was performed to rule out the possibility of organic obstruction or peptic ulcer disease. None of the subjects had undergone previous surgery of the GI tract or were taking any medications known to be associated with nausea, vomiting, or dyspepsia (e.g., nonsteroidal anti-inflammatory drugs, digoxin, etc.). None of the postmenopausal women were on hormone replacement therapy. Informed consent was obtained from all subjects, and the ethics review committee of the Taichung Veterans General Hospital approved the study protocol.

Electrical Stimulation of the Acupuncture Points

Electrical stimulation of the acupuncture points was performed in the subjects using acupuncture needles. Two acupuncture needles (0.3 mm in diameter, 30 mm long; Chian-Huei Acupuncture Appliance, Taipei, Taiwan) were inserted into the subject's legs at the Zusanli (St 36) points and manipulated until a 'chi' sensation (a deep cramp-like sensation) was reported. The Zusanli points are located about 10 cm below the patella and 2 cm lateral from the anterior rest of the tibia. The acupuncture needles were connected to a 9-volt battery-powered electrical acupuncture instrument (model 04S; Gwo-Jih Medical Instruments, Taipei). Biphasic, square electrical stimula-

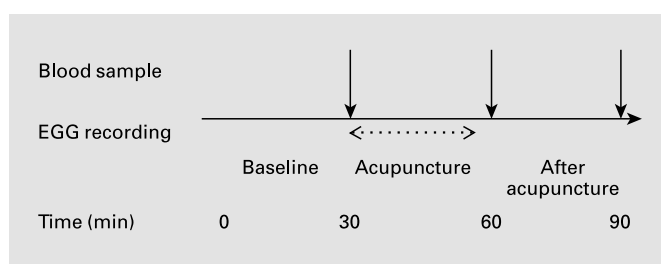


Fig. 1. Study protocol.

tion using 2-Hz pulses with a wave width of 0.16 ms at the maximal tolerated strength without discomfort was delivered for 30 min (fig. 1).

Electrogastrography (EGG)

Cutaneous EGG was performed in the morning after an overnight fast for 30 min in the baseline state, 30 min during acupuncture, and for an additional 30 min after acupuncture. The subjects were positioned comfortably in a chair and were requested to remain as still as possible to reduce motion artifacts. After gentle skin abrasion to enhance electrical condition, three Ag-AgCl electrodes (Accutac Diaphoretic ECG Electrodes; NDM, Dayton, Ohio, USA) were affixed to the abdomen. The first electrode, for one of the active EGG leads, was placed on the patient's left side about one third of the distance from the ventral to the left axial midline and 1 cm below the bottom rib. The second electrode, for the other active EGG lead, was placed on the patient's ventral midline about halfway between the umbilicus and the xyphoid process. The third electrode, for the reference lead, was placed on the patient's abdomen, forming a triangle with three equal sides.

EGG was performed with a portable EGG recorder (Synetics Medical, Irving, Tex., USA). All recordings in the study were made at sampling frequencies of 4 Hz. After measurement, the EGG data were digitized, fed into a personal computer, and analyzed by means of a commercially available software (ElectroGastroGram version 6.30; Gastrosoft/Synetics Medical). Motion artifacts (large amplitude deflections) on the original EGG recording were identified visually and deleted before analysis. To avoid any artifact during acupuncture needle insertion and initiation of electrical stimulation, EGG analysis was conducted for 20 min during each period (to exclude the first and last 5 min from each 30-min period). The data were obtained by running spectrum analysis. Using a fast Fourier transform algorithm of a 256-second 'window' of the raw data, power spectra of overlapping stretches for 192 s between the subsequent stretches of the electric signal were computed and displayed as a function of time, yielding frequency and amplitude information over the course of the study [13]. Several variables, including the dominant frequency (DF), the percentages of DF in the defined normal frequency range (2–4 cpm), the bradygastric range (0.5–2 cpm) and the tachygastric range (4–9 cpm), the DF instability coefficient (DFIC), and the dominant power instability coefficient (DPIC) were analyzed. Any DF higher than 10 cpm was separated from tachygastric, because it was assumed to arise from outside the stomach. The DF was calculated as the highest peak of the mean fast Fourier transform line during the recording time. The DFIC was used to ascertain the changes in DF during the period of data acquisition. It was

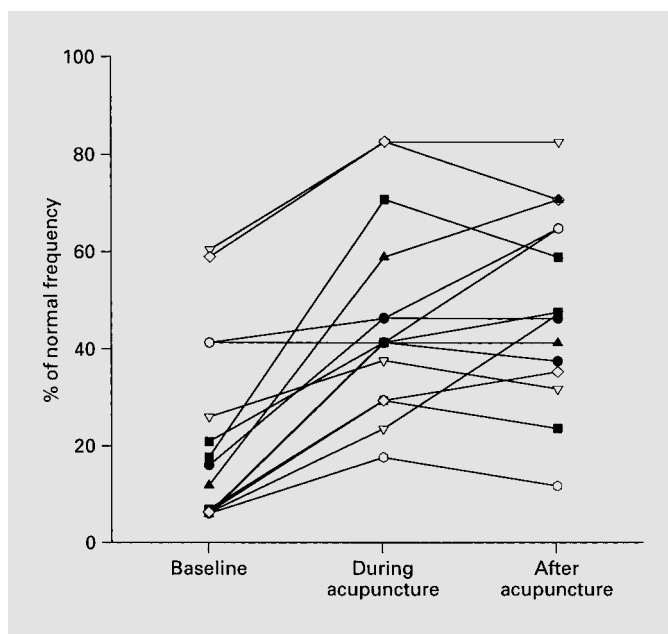


Fig. 2. Percentage of normal frequency at baseline and during and after acupuncture.

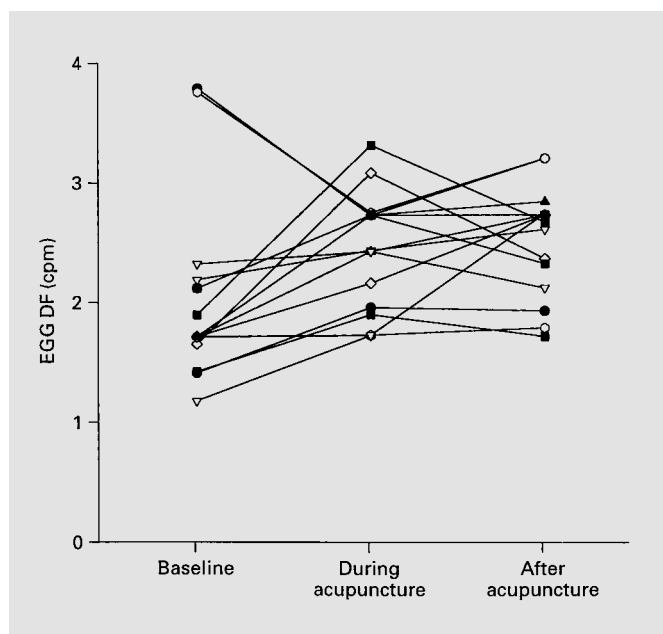


Fig. 3. EGG DF at baseline and during and after acupuncture.

Table 1. EGG parameters at baseline and during and after acupuncture

	Baseline	Acupuncture	After acupuncture
DF, cpm	2.03 ± 0.76	2.43 ± 0.47*	2.49 ± 0.46*
DF in normal range, %	21.99 ± 19.38	45.93 ± 19.72**	48.92 ± 19.56**
Bradygastria, %	59.02 ± 29.97	48.67 ± 20.14	44.79 ± 22.15
Tachygastria, %	20.32 ± 19.60	5.40 ± 8.41**	6.29 ± 7.41**
DFIC, %	58.07 ± 29.44	51.73 ± 16.00	47.07 ± 13.75
DPIC, %	106.47 ± 62.90	97.73 ± 55.47	124.7 ± 55.13
PR	1	1.05 ± 0.60	1.12 ± 0.56

* $p < 0.05$ by paired t test, during or after acupuncture versus baseline; ** $p < 0.01$ by paired t test, during or after acupuncture versus baseline.

Table 2. Serum blood glucose, gastrin, motilin, and hPP levels at baseline and during and after acupuncture

	Baseline	Acupuncture	After acupuncture
Glucose, mg/dl	138.73 ± 43.39	135.40 ± 43.04	134.27 ± 46.32
Gastrin, ng/ml	68.26 ± 21.92	67.41 ± 21.27	69.41 ± 16.52
Motilin, pmol/l	28.46 ± 8.11	27.32 ± 7.83	24.48 ± 4.90
hPP, pmol/l	56.96 ± 27.64	73.11 ± 22.37*	63.46 ± 26.31

* $p < 0.05$ by paired t test, acupuncture versus baseline.

defined as the coefficient of variation (standard deviation/mean DF $\times 100\%$) of DF. In addition, the DPIC was used to ascertain the changes in dominant power (DP) during the period of data acquisition. It was defined as the coefficient of variation (standard deviation/mean DP $\times 100\%$) of DP. The DP during and after acupuncture was compared with the DP during the baseline period to yield the power ratio (PR) for the acupuncture period and the period after acupuncture. Therefore, the PR at the baseline was defined as 1 for comparison.

Assay of Serum GI Hormones

Serum gastrin, motilin, and hPP levels were measured with commercial ELISA kits (Euro-Diagnostica, Malmö, Sweden). Ten milliliters of blood was collected at 30-min intervals at the end of each stage (i.e., baseline, acupuncture, and stage after acupuncture). Venous blood was collected in tubes without additives. The blood samples were placed on ice and centrifuged at 4°C and 3,000 rpm for 10 min. The serum was separated and stored below -20°C before analysis. Serum values were expressed as nanograms per milliliter for gastrin and as picomoles per liter for motilin and hPP. In addition, blood glucose levels were also evaluated at each stage.

Statistical Analysis

Data are expressed as mean values $\pm$ SD. Statistical analyses were performed to investigate the effects of acupuncture on EGG parameters and blood glucose as well as GI hormones, using repeated analysis of variance and a paired *t* test. $p < 0.05$ was considered statistically significant.

Results

With 2 Hz of electrical stimulation of the Zusanli points, there was a significant increase in the percentages of normal frequency during and after acupuncture (baseline vs. during and after acupuncture $21.99 \pm 19.38\%$ vs. 45.93 ± 19.72 and $48.92 \pm 19.56\%$, $p < 0.01$; fig. 2). In addition, the percentages of tachygastric frequency were decreased significantly during and after acupuncture (baseline vs. during and after acupuncture $20.32 \pm 19.60\%$ vs. 5.40 ± 8.41 and $6.29 \pm 7.41\%$, $p < 0.01$; table 1). The DF was also changed significantly (baseline vs. during and after acupuncture 2.03 ± 0.76 cpm vs. 2.43 ± 0.47 and 2.49 ± 0.46 cpm, $p < 0.05$; fig. 3). However, the changes in percentages of bradygastric frequency, DFIC, DPIC, and PR were not statistically significant, either during or after acupuncture.

The blood glucose levels did not change significantly during each study period (baseline vs. acupuncture and period after acupuncture 138.73 ± 43.39 mg/dl vs. 135.40 ± 43.04 and 134.27 ± 46.32 mg/dl, no significance). In addition, the serum levels of gastrin and motilin did not change during each study period (table 2). However, there was a significant increase in serum hPP

during acupuncture (baseline vs. acupuncture 56.96 ± 27.64 pmol/l vs. 73.11 ± 22.37 pmol/l, $p < 0.05$). The serum level of hPP after acupuncture was also higher, but this was not statistically significant (baseline vs. after acupuncture 56.96 ± 27.64 pmol/l vs. 63.46 ± 26.31 pmol/l, no significance).

No adverse effects were noted during or after acupuncture. Although all the patients had experienced dyspeptic symptoms during the 3 months prior the study, no significant change in the symptoms was reported immediately after the investigation.

Discussion

The results of this study revealed that acupuncture at the Zusanli points could increase the percentage of normal EGG frequency and decrease the percentage of tachygastric frequency in diabetic patients with dyspeptic symptoms. The DF was also improved during and after acupuncture. The data indicate that acupuncture may enhance the regularity of gastric myoelectrical activity in diabetic patients with dyspeptic symptoms.

The role of EGG in clinical gastroenterology has not yet been clearly defined [14–17]. EGG has been proven by some authors to provide useful information for the clinical diagnosis [18]. EGG abnormalities have been described in disorders of gastric emptying, nausea and vomiting in pregnancy [19], motion sickness [20, 21], anorexia nervosa [22], chronic intestinal pseudo-obstruction [23, 24], and diabetic gastroparesis [5]. Phasic contraction of the distal stomach is coordinated by a rhythmic electrical depolarization, known as the pacemaker potential or gastric slow wave, which is generated in the proximal gastric body. Under normal conditions, the slow wave oscillates at 3 cpm. However, certain rhythm disturbances have been described in clinical disease, such as an overly fast rhythm (tachygastria), an overly slow rhythm (bradygastria), and an irregular rhythm (arrhythmia) [14]. Tachygastria and bradygastria are found in many patients with severe diabetic gastroparesis [3, 4]. In this study, all the diabetic patients with dyspeptic symptoms showed a decrease in the percentage of normal frequency and an increase of both bradygastria and tachygastria. After one 30-min session of acupuncture, there was a significant improvement in gastric myoelectrical activity. Nevertheless, after 30 min of acupuncture, the percentage of normal frequency was still outside the normal range.

Studies published in the Chinese literature have reported improvement of gastrointestinal motility and

symptoms with acupuncture [25]. Acupuncture at the Neiguan point in patients who underwent gynecological surgery had a significant antiemetic effect on postoperative nausea and vomiting [9], and it could also decrease cisplatin-associated nausea and vomiting in cancer patients [10]. Electrical acu-stimulation of the Neiguan point reduced the severity of symptoms of motion sickness and decreased gastric tachyarrhythmia [26]. The present study is the first report in the literature involving the application of electrical stimulation at Zusanli points in diabetic patients, and it revealed an improvement in gastric myoelectrical activity. It is possible that dysrhythmias are symptomatically important in diabetic gastroparesis because the correction of the slow-wave disturbance, but not the gastric emptying defect, correlates best with a reduction in nausea [3]. The impact of acupuncture on GI function is complex, and results depend upon the species studied, the acupuncture points employed, the methods of manipulation, and the underlying functional activity of the gut. Results of acupuncture analgesia studies suggest that high-frequency electrical stimulation of acupuncture points predominantly is associated with local effects of short duration on pain perception and tolerance [27]. Low-frequency stimulation of 1–4 Hz often is associated with effects that are less localized and of longer duration. In addition, Dundee et al. [28] reported that a 10-Hz stimulation at P6 was better than 100 Hz in reducing postoperative nausea and vomiting. Therefore, in this study, we used a low frequency of electrical stimulation (2 Hz) at the Zusanli points. However, in clinical practice, it generally takes several sessions of acupuncture to achieve a favorable effect [28]. So, it was reasonable that there was only a moderate improvement in the EGG parameters and no immediate change in the dyspeptic symptoms after one session of acupuncture in this study.

For further understanding the effects of acupuncture on gastric myoelectrical activity, we evaluated blood glucose and several GI hormones, including gastrin, motilin, and hPP, before, during, and after acupuncture. Motilin is a 22 amino acid polypeptide, secreted from endocrine cells of the small intestinal mucosa, which stimulates the contraction of smooth muscle in the GI tract [29]. While most of the GI hormones are released in response to the ingestion of a meal, motilin has the following specific characteristics: it is released at about 100-min intervals during the interdigestive state, when no nutrient is present, at least in the duodenum and the upper jejunum, and moreover the release of motilin is inhibited by feeding in dogs [30] and humans [31]. The participation of vagal control in the release of motilin has been controver-

sial, but because chronic truncal vagotomy fails to affect motilin release [32], the release of motilin is likely to be controlled by nonvagal cholinergic innervation. In our study, the serum levels of motilin did not change during each study period. These data might indicate that motilin did not play a role in the effect of acupuncture on gastric myoelectrical activity.

The release of gastrin from antral G cells is regulated by luminal, paracrine, endocrine, and neural stimuli [33]. Parasympathetic innervation by the vagus nerve exerts a complex effect on gastrin release. Gastrin may stimulate the contraction of gastric smooth muscle and increase gastric emptying. Infusion of physiological doses of gastrin increases amplitude and frequency of antral contractions, with an associated increase in the pacesetter potential frequency and percentage of pacesetter potentials that reach a contractile threshold [34]. In our study, the serum levels of gastrin did not change during all study periods. This might also indicate that gastrin did not play a role in the effect of acupuncture on the gastric myoelectrical activity.

hPP is a 36 amino acid peptide hormone with a molecular weight of 4,200 produced in the pancreas [35]. The physiological role of hPP includes the inhibition of stimulated gastric and pancreatic exocrine secretions and the augmentation of insulin-inhibited hepatic glucose production. hPP is released from the endocrine pancreas after ingestion of a meal via vagal, cholinergic mechanisms [35]. The secretion of hPP is affected by several different physiologic stimuli, such as food intake and fluctuations in blood glucose concentration. However, one key regulatory mechanism, vagal cholinergic stimulation, seems to govern the release of the peptide [36, 37]. Based on the fact that hPP secretion is dependent upon cholinergic tone, it has been suggested that hPP might serve as an independent indicator of abdominal vagal tone in the basal state [38]. A reduced release of hPP after sham feeding has been observed in some patients with functional dyspepsia, implicating impaired efferent cholinergic vagal function [39]. There was a significant increase in serum hPP during acupuncture. Although the serum level of hPP after acupuncture was also higher, this was not statistically significant. However, the increase in hPP after acupuncture observed in this study was much less than that caused by other stimuli, such as food intake and fluctuations in blood glucose concentrations. The role of serum hPP in the effect of acupuncture on gastric myoelectrical activity needs further investigation. However, there is evidence supporting vagally mediated mechanisms for electroacupuncture at the Zusanli points to affect gastric acid secretion [40, 41].

The effect of blood glucose levels on gastric myoelectrical activities has been judiciously studied. With hyperglycemic clamping in healthy volunteers, a plasma glucose threshold of approximately 175 mg/dl was shown to inhibit postprandial phasic antral motor activity [42]. Furthermore, with an increase in the plasma glucose level to 230 mg/dl, disruption of gastric slow-wave cycling was observed, with marked increases in both tachygastric and arrhythmic activities. Therefore, the authors concluded that underlying neuropathy or myopathy is not necessary for impairment of gastric myoelectrical activity in diabetic patients. In this study, all patients showed evidence of autonomic neuropathy. The blood glucose levels did not change significantly before, during, or after acupuncture in our study. Therefore, the improvement in gastric dysrhythmia in diabetic patients in this study may have been due to the direct effect of acupuncture on gastric myoelectrical activity rather than the effect of blood glucose.

In conclusion, the results of this study indicate that acupuncture may enhance the regularity of gastric myoelectrical activity in diabetic patients with dyspeptic symptoms. The effect of acupuncture on gastric myoelectrical activities was not correlated with changes in blood glucose, gastrin, or motilin. Although there was an increase in hPP levels during acupuncture, its role in the effect of acupuncture on gastric myoelectrical activities is still obscure. Further study is required to clarify the effect of long-term acupuncture treatment on gastric dysrhythmia.

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