RAPID COMMUNICATION

Holistic Acupuncture approach to idiopathic refractory nausea, abdominal pain and bloating

Ann Ouyang, Lihua Xu

Ann Ouyang, Lihua Xu, Division of Gastroenterology and Hepatology, Department of Medicine, The Milton S. Hershey Medical Center, College of Medicine, Pennsylvania State University, Hershey, PA 17033, United States
Correspondence to: Ann Ouyang, MD, H045, Division of Gastroenterology and Hepatology, The Milton S. Hershey Medical Center, 500 University Drive, Hershey, PA 17033, United States. aouyang@psu.edu
Telephone: +1-717-5318741 Fax: +1-717-5316770
Received: May 29, 2007 Revised: August 8, 2007

© 2007 WJG. All rights reserved.

Key words: Acupuncture; Functional bowel disorder; nausea; Pain; Holistic medicine

Ouyang A, Xu L. Holistic Acupuncture approach to idiopathic refractory nausea, abdominal pain and bloating. *World J Gastroenterol* 2007; 13(40): 5360-5366

<http://www.wjgnet.com/1007-9327/13/5360.asp>

Abstract

AIM: To evaluate the effectiveness of a holistic acupuncture approach on nausea, pain, bloating and electrogastrogram (EGG) parameters in patients with intractable symptoms.

METHODS: Twelve patients with no or mild nausea (those without nausea had bloating or pain) and 10 with a history of moderate to severe nausea were referred for acupuncture. All underwent an EGG and were treated at acupuncture points PC6, SP4 and DU20. Visual analog scales (VAS) assessing severity of nausea, pain and bloating were obtained before and after acupuncture treatment. Nineteen patients received three and three patients received two treatments.

RESULTS: VAS scores for nausea reflected the clinical assessment and differed significantly between mild and moderate/severe nausea groups. Acupuncture significantly improved severity of nausea in both groups with improved pre-treatment nausea between the first and third treatments in the moderate/severe nausea group. Pain scores improved with acupuncture in the mild nausea group only and bloating improved only with the first treatment in this group. Patients with bloating with VAS scores greater than 35 pre-treatment improved with acupuncture and over all VAS scores for pain improved with treatment. Acupuncture increased the power in the 2.7 to 3.5 cpm range in the EGG.

CONCLUSION: In this uncontrolled clinical study, a holistic acupuncture approach significantly improved nausea in patients with refractory symptoms and increased the power in the 2.7-3.5 cpm component of the electrogastrogram. Bloating and pain VAS scores improved acutely with treatment. This study suggests that acupuncture may be effective in this refractory group of patients and further study using appropriate controls is warranted.

INTRODUCTION

Nausea is a debilitating symptom that severely impacts on quality of life. Surveys of patients with functional dyspepsia (chronic or recurrent abdominal pain without an anatomic or inflammatory cause) and patients undergoing chemotherapy, identify nausea as one of the symptoms with the greatest negative impact on quality of life^[1,2]. It is a complicated symptom to study and treat because it is often a co-morbid symptom and multiple factors impact on its etiology and severity.

Nausea is a prominent symptom in approximately 20% of patients recruited to dyspepsia studies in whom pain is the major complaint^[1]. Patients who present with chronic or recurrent nausea in whom no biochemical, anatomic or inflammatory abnormalities can be found, are diagnosed as having functional nausea^[3]. Efforts to determine a single pathophysiologic process in patients with functional nausea have been unsuccessful. Some patients have gastroparesis, or delayed emptying of solid foods from the stomach, either related to other medical conditions such as diabetes mellitus or without any obvious underlying systemic disorder. Others have normal gastric emptying despite severe nausea. Even when a condition such as gastroparesis is identified, it is unclear whether the symptom of nausea can be directly ascribed to that condition^[4]. Symptoms of nausea can vary in severity over time despite persistent delayed gastric emptying, suggesting that gastroparesis alone does not explain the severity of nausea. Medications for treatment of nausea are limited to those that increase gastric or duodenal contractile activity, the prokinetic agents, and those affecting the chemoreceptor trigger zone^[3]. Many prokinetic and centrally acting medications have significant side effects. Psychological factors are often important. Even following chemotherapy, a condition where nausea is known to be a direct effect of medications, the severity of nausea is impacted by psychological stress from family

relations^[5]. Psychotropic agents may be helpful in the treatment of nausea, but many have side effects that may be counterproductive to gastric function, such as the anticholinergic action of tricyclic antidepressants.

The complexity of the processes contributing to nausea does not lend itself to the usual "modern" medical approach to disease, which includes treating each abnormal condition with separate medications. In contrast, the ancient Chinese paradigm of medicine involves a holistic approach that uses a paradigm of deviation from balance in energy or "Qi" and accepts the concept that many conditions that would appear to involve disparate organ systems may be intertwined resulting in "imbalance". Improvement in symptoms requires the treatment of multiple conditions to restore balance^[6].

Acupuncture has been used since antiquity to treat patients with nausea^[7] and has been subjected to clinical study. It has been used with moderate success in patients with chemotherapy induced nausea and post-operative nausea^[7,8,9]. A search of the literature revealed no reports of its use in treating functional nausea.

The aims of this study were to examine the effect of acupuncture, using a holistic approach, in patients referred for nausea and/or abdominal pain, refractory to routine medical treatment. We examined the effect on the symptoms of nausea, bloating, and pain and on gastric motor activity, as assessed by electrogastrography. The holistic approach included acupuncture therapy at three points, PC6, SP4 and DU20. These are described in detail in the methods section.

MATERIALS AND METHODS

Subjects and treatment

Charts were reviewed of 22 patients (3 male, 19 female. Mean 44.1 ± 2.7 years, range 17-66) who were treated with acupuncture between June 2003 and December 2005. Patients were referred to Hershey Medical Center for care and treatment with prokinetic agents and usual therapy had failed. All patients were interested in pursuing alternative medical therapy. All patients had undergone the same treatment plan. Charts were reviewed for the history of the severity and duration of nausea, abdominal pain and bloating and prior gastric emptying studies. Fourteen of the patients had a documented diagnosis of depression on their chart. The other patients had no documentation of psychiatric disorders but no documentation stated specifically that there were no psychological issues. From the chart narrative, patients were determined to have either no nausea or mild nausea (those with no nausea complained primarily of abdominal bloating and pain) or moderate to severe nausea. The severity of each symptom was also assessed before and after each acupuncture treatment using a visual analog scale (VAS) with 0 for no symptoms and 100 for the worst symptom during the first three treatments. The assessment by the physician in clinic was not known to the subject who completed the VAS score and was based on patients' history of the complaint. EGGs were also performed on all patients^[10]. During the treatment sessions, the acupuncture points P6, SP4 bilaterally and DU20 were needled for 30 min, while the EGG was recorded. A

VAS was completed for each of the symptoms of nausea, pain and bloating before and after each acupuncture treatment. Patients returned for at least one or two additional treatments. Nineteen patients had three treatment and three patients underwent two treatments. The average duration between treatments was 15 ± 1.9 d (mean $\pm$ SE), range 7-33 d. The study was approved by the Institutional Review Board of the Hershey Medical Center (November 8, 2006).

Electrogastrogram (EGG) recording and analysis

All patients underwent a clinical EGG following our standard protocol^[10]. Patients fasted overnight. On the day of treatment, each patient consumed a standard 200 Kcal snack of 8oz of apple juice and two slices of toast. Each subject then fasted for an additional two hours after which time EGG recordings were obtained. On the first treatment day, a water load test was performed after 15 min of baseline EGG. EGG recording was then continued during the 30 min of acupuncture treatment. Signals were passed through 0.016 Hz high-pass filter and a 0.25 Hz low-pass filter. The EGG signal was reviewed to remove areas of artifact and the resulting EGG signal was digitized for computer analysis and subjected to fast Fourier transform to extract the frequency information present in the EGG signal. A running spectral analysis of the component wave form was followed over time. The percent power in the frequency ranges of 1.0-2.5 cpm, 2.5-3.7 cpm and 3.7 to 10 cpm were recorded.

Water load test

A water load test was performed at the first treatment session. After a 15 min baseline EGG was recorded, the patients ingested water "until full" within five minutes. The water was non-carbonated spring water at room temperature (23°C). The volume (mL) of water drunk was recorded^[10].

Visual analog scale (VAS) for symptoms

A visual analog scale (VAS) with a score from 0-100 points was utilized to assess the intensity of each of the following visceral sensations: nausea, pain, bloating, with 0 being none and 100 being unbearable. Each subject completed a VAS score prior to the study and before and after each acupuncture treatment.

Acupuncture points

Acupuncture points P6, SP4 and DU20 were selected for this treatment regimen^[7]. The point PC6 (Neiguan) is on the pericardium meridian of hand-jueyin. It is located 2 cm above the transverse crease of the wrist, between the tendons of *muscularis palmaris longus* and the *flexor radialis*. The traditional indications for needling of the PC6 point are stomach ache, nausea, vomiting, hiccough, mental disorders, epilepsy, insomnia, febrile disease, irritability, and malaria. The point SP4 (Gong sun) lies on the Spleen meridian of the foot-taiyin. It is located in the depression distal and inferior to the base of the first metatarsal bone. The traditional indications for treatment of the SP4 point relate to the gastrointestinal (GI) or central nervous system and are abdominal pain and distension, diarrhea, dysentery,

Table 1 Demographics and clinical characteristics of patients in the mild or severe nausea groups

	Mild nausea (<i>n</i> = 12) symptom score 0 or 1	Severe nausea (<i>n</i> = 10) symptom score 2 or 3	<i>P</i>
Gender	10F:1M	9F:1M	NS
Age (yr ± SE)	47.5 ± 2.9	40 ± 4.6	NS
Weight (lbs ± SE)	143 ± 7	150.8 ± 10.4	NS
Diabetes	1/12	1/10	
Severity of nausea ¹	0.25 ± 0.04	2.6 ± 0.15	<i>P</i> < 0.0001
Severity of pain ¹	2 ± 0.3	1.1 ± 0.37	NS
Severity of bloating ¹	2.3 ± 0.37	1.2 ± 0.5	NS
Duration of symptoms in months (mean ± SE)	24.9 ± 5 Range 7-60	15.3 ± 3.4 Range 4-36	NS ²

¹Symptom key: 0-none, 1-mild, 2-moderate, 3-severe (based on narrative and complaint in patient chart). ²Using Mann-Whitney test for non-parametric data.

borborygmus, nausea, vomiting, hiccough, and insomnia. The point DU20 (Baihui or GV 20) lies on the Governor vessel. It is located in the midline of the head, at the intersection of the line connecting the apices of both ears and a line that lies in the midline in the sagittal orientation on the head. The traditional indications for using the DU20 point are vertigo, headache, tinnitus, nasal obstruction, aphasia by apoplexy, coma, mental disorders, prolapse of the rectum and the uterus. It was felt that this combination of points would treat specific nausea symptoms and gastrointestinal complaints as well as depression, which was felt to be a common problem for many patients with refractory nausea.

Statistical analysis

The charts were reviewed for age, weight, gender, and assessment of the severity of the symptoms of nausea, vomiting, bloating and pain at the clinic visit. As the degree of nausea was variable patients were analyzed in two groups based on the severity of nausea determined by history at the initial clinic assessment-either in a "none to mild" nausea group or a "moderate to severe" nausea group. Separation of patients into the two groups was based on clinical assessment of the chart and was determined prior to any knowledge of the outcome of treatment.

The effect of acupuncture before and after treatment in the different groups and its effect on the parameters of VAS scores for nausea, bloating and pain and power of EGG in the different frequencies was analyzed using ANOVA. If a significance level of *P* < 0.05 was determined, direct comparisons between specific parameters was performed using a student *t* test (two-tailed) for parametric data or Mann-Whitney test for non-parametric data. Data are presented as mean ± SE.

RESULTS

Patients were primarily analyzed as two groups, based on

Figure 1 VAS score for symptoms of nausea, abdominal pain and bloating at baseline for patients in either the mild or severe nausea groups. A significant difference was seen in the VAS score for nausea between the groups (*P* = 0.0002).

an assessment of the severity of nausea as determined by obtaining a history from patients at their initial clinic visit. Those with no or mild nausea were grouped in the mild nausea group (*n* = 12), those with moderate or severe nausea were grouped in the severe nausea group (*n* = 10). The demographics and clinical features are shown in Table 1. In the group who complained of mild to no nausea, nine patients did not complain of nausea, but complained more of pain and/or bloating. The frequency of nausea (25% vs 100%) and the severity of nausea was significantly different between the groups (*P* < 0.05). There was no difference in either the prevalence of abdominal pain or bloating or severity of these symptoms between the two groups. The duration of nausea when present was between seven months and five years in the mild nausea group and between four months and three years in the severe nausea group (not significant [NS]). Only one out of each group was diabetic.

At the first visit for acupuncture treatment, the VAS scores for nausea were significantly greater in the severe nausea group than the mild nausea group (68.2 ± 4.4 vs 33.3 ± 5.8 , *P* < 0.0002, Figure 1) and these subjects tolerated the water load test more poorly than did the mild nausea group (429 ± 33.9 vs 642 ± 22 mL, *P* < 0.0001). There was no significant difference in VAS scores for bloating or pain at baseline between the two groups. Bloating was the predominant symptom in the mild nausea group while both nausea and bloating were equally prominent in the severe nausea group.

Effect of acupuncture on symptoms

Acupuncture significantly improved the VAS score for nausea in both the mild nausea and severe nausea groups (Figure 2A). There was improvement in the pre-acupuncture nausea score between the first and third treatment in the severe nausea group (*P* < 0.03) suggesting a persistent effect between treatments. In the mild nausea group, there was no significant difference in the baseline score between the first and third treatment.

Acupuncture was less effective for the symptoms of pain or bloating (Figure 2B and C). Pain scores were significantly improved during acupuncture in the mild nausea

Figure 2 Effect of acupuncture on the symptoms of nausea (A), abdominal pain (B) and bloating (C) in the patients with mild or severe nausea. The response to each acupuncture treatment is shown.

group. No significant improvement was seen in the severe nausea group although the trend was towards improvement. Although bloating improved during the first acupuncture treatment in the mild nausea group, no significant improvement was seen in the severe nausea group.

Additional categorization of patients examined the response of bloating and pain to acupuncture by the pre-treatment VAS score, as the examining physician did not score the symptoms of pain and bloating clinically. The VAS for bloating improved with the first acupuncture treatment ($n = 22$) from 56.2 ± 7.7 to 30.4 ± 5.4 ($P < 0.01$). The overall pain score for all patients decreased from 35.9 ± 7.8 to 17.8 ± 0.8 ($P = 0.08$) with the first treatment. We also compared responses to acupuncture in patients with mild vs moderate/severe symptoms of bloating or pain.

Figure 3 Effect of acupuncture on the symptoms of bloating and pain. Response of patients with a baseline pre-treatment VAS of > 35 (moderate/severe) or ≤ 35 (mild) are shown. The numbers of patients in each group are shown for each treatment session. A significant improvement was seen with acupuncture at the first treatment only for bloating although there was a significant decrease in pre-treatment bloating between the first and third treatment. Acupuncture improved pain with most treatments but the improvement was not sustained.

We chose an arbitrary cut off of an initial VAS score of 35 out of 100 to differentiate patients with mild bloating or pain from those with moderate or severe bloating or pain (Figure 3). The VAS for bloating improved with initial treatment in those with a baseline VAS score of greater than 35. While there was no acute improvement with subsequent treatments, there was a significant improvement in the pre-treatment VAS for bloating over the three treatments (Figure 3). Acupuncture treatment resulted in improvement of the VAS score for pain in both those with severe/moderate pain and mild pain after the acute acupuncture treatment (Figure 3). However, there was no significant improvement in pre-treatment pain between the first and third treatments.

Effect of acupuncture on EGG

Acupuncture resulted in a significant improvement in the percent of power in the normal frequency. At baseline, there was no difference in overall EGG diagnosis between the severe and mild nausea groups. When comparing the power in the different frequency components before and after acupuncture, there was a significant improvement in the power in the 2.5-3.7 cpm between the pre-acupuncture

and post-acupuncture EGG following the first and second treatments in the severe nausea patients. The percent power in this range improved from 23.4 ± 7.5 to 30.8 ± 10 following the first treatment ($P < 0.05$) and from 19.35 ± 10 to 31.2 ± 10.8 with the second treatment ($P < 0.03$). The third treatment increased the percent power in this frequency range from 28.1 ± 11.3 to 37.3 ± 15 (NS). In the mild nausea group, the percent power in this normal frequency range also improved comparing pre- and post-acupuncture treatment but did not reach statistical significance. There was no correlation between the percent power in the 2.5-3.7 cpm range and the symptoms of bloating or pain.

DISCUSSION

We report the results of our experience with the use of acupuncture in patients with functional dyspepsia and nausea. A significant improvement in the level of nausea was seen following acupuncture in patients with none to mild nausea (mild nausea group) and those who complained of moderate to severe nausea (severe nausea group). A significant response was seen in both, suggesting that acupuncture given in the holistic method was effective for both mild to severe nausea. Only one patient in each group was diabetic and most had failed other treatment modalities. A review of Pubmed using the search term "acupuncture and nausea" revealed no prior reports of the use of acupuncture for functional dyspepsia or nausea, other than one study of 15 patients with diabetes and symptoms suggestive of gastric dysmotility^[11]. There was a significant improvement in the VAS score for pain in the mild nausea group and the first treatment only improved bloating in the mild nausea group. This difference in response between complaints of nausea and the other complaints of pain and bloating suggest that the response seen was not purely placebo. This is also the first reported study in which acupuncture was given in a holistic approach for nausea.

Multiple studies report the use of acupuncture in the treatment of chemotherapy induced nausea, post-operative nausea and nausea in pregnancy. Acupuncture is effective in most studies without controls, but its effectiveness is less noticeable if compared to a placebo or sham treatment^[7-9]. Controlled studies of acupuncture in the treatment of chemotherapy induced nausea and vomiting suggest a moderate effect with less acute vomiting episodes and an improvement in the mean worst nausea severity in patients treated by acupressure and concurrent anti-emetics^[8]. Following elective gynecological surgery, a greater percentage of patients treated with acupressure of PC6 point (also known as P6 point) reported no nausea or vomiting compared to sham treated patients^[9]. Several studies suggest effectiveness of acupuncture/acupressure in treating nausea of pregnancy. A randomized controlled trial of acupressure at P6 *vs* placebo showed improvement of symptoms of nausea over time in both groups with nausea symptoms being less severe in the acupressure treated group^[12]. Others report an improvement in duration but not intensity of nausea in pregnancy compared to placebo treatment^[13]. Although well-conducted placebo controlled studies failed to show a difference compared to

sham treatment, acupuncture may prove to be as effective as medications^[13,14].

Comparison between studies is difficult because the criteria for recruitment of subjects and presence of potentially confounding factors, such as depression, are often not discussed. Most of the trials involve acupuncture at one or two acupuncture points only, mainly P6, and are therefore different from the usual clinical holistic approach when using acupuncture to treat a patient. A review of several studies suggests that these studies may be under-powered and a true difference between placebo and sham may be missed^[15].

Our treatment included acupuncture at three points, two related to the GI tract and one at a point recommended for psychological complaints. These points were chosen based on clinical experience and training and our observation that many of the subjects with nausea have psychological distress. We did not formally test for any psychiatric diagnosis, as this was a clinical treatment approach. The results suggest that acupuncture at the points chosen for this study may be effective in treating nausea and less for pain or bloating when patients are grouped by degree of nausea. When the subjects are grouped into moderate/severe or mild bloating or pain by their first pre-treatment VAS score, an improvement in VAS score was seen in bloating and pain. It is unclear if this can be extrapolated to treatment of functional bloating or pain as the degree of symptom was assessed by the pre-treatment VAS score and it is unknown if this correlates with the degree of chronic symptom complaint. There was an increase in the power of gastric myoelectric activity in the normal range, 2.5-3.7 cpm, as assessed by EGG. Whether this is a primary effect of acupuncture or secondary to a central nervous system response cannot be determined in this study. These data support further study using a placebo-controlled approach.

The mechanism of the action of acupuncture is unknown. There are few studies in patients examining the effect in nausea in humans. Hu *et al*^[16] demonstrated that acupressure at the PC6 point decreased symptoms of nausea and decreased the gastric dysrhythmia induced byvection in an optokinetic drum. An increase in the percent of normal frequency in the EGG has been reported in diabetic patients with symptoms suggesting an action of acupuncture on gastric motor function^[17]. In these subjects, the ST36 points and electrical stimulation of needles was used. In humans, acupuncture and manipulation at the PC6 point in healthy volunteers selectively activated regions of the superior frontal gyrus, anterior cingulate gyrus and dorsomedial nucleus of the thalamus as well as areas of the cerebellum^[17]. The subjects did experience more unpleasantness with active acupuncture than with sham treatment which may explain the cerebral cortical findings. The cerebellar findings may be more specific to the action of acupuncture at PC6, as activation of this brain area is probably unrelated to the pain of needle placement.

In animals, acupuncture of the PC6 and ST36 points results in an increased rate of gastric emptying and an increase in the percent of time that the dominant frequency is within the normal range^[18]. Based on the effect of acupuncture on the heart rate variability, it was concluded that this effect was associated with increased vagal activity. A

central effect of electroacupuncture has also been suggested by Tatewaki *et al.*^[19] who demonstrated that electroacupuncture at PC6 reduced the number of retching and vomiting episodes following vasopressin injection in dogs, an anti-emetic effect which was abolished by pretreatment with naloxone. Whether this proves to be similar for humans is unknown. The effect of acupuncture is complex in animals, with studies showing that in the rat, electrical stimulation of the ST36 point can induce either excitatory or inhibitory effects on gastric contraction^[20]. Multiple variables are possible to explain differences in animals: the site of stimulation and the intensity and type of stimulation. These effects in animals support a true physiologic response to stimulation of acupuncture points.

In humans, additional variables are present. These include co-morbid conditions, particularly other pain or psychological conditions. The effect may be influenced by belief in the treatment that may contribute to a placebo effect, or may be associated with central nervous system biological responses that may impact on response to acupuncture *via* a non-placebo mechanism. For example, a study by Pariente *et al.*^[21] demonstrated that real acupuncture stimulated activity in the brain, as assessed by fMRI, to a greater extent than placebo and that belief in acupuncture affected the response at other areas of the brain. Our clinical study was not designed to test the effect of placebo or belief in the response. However, the differential effect of acupuncture on the symptoms of nausea compared to pain and bloating in the same subjects suggests that the effect on nausea may not be entirely placebo. These results would support the value of a rigorously designed study to examine the effects of acupuncture on the symptoms of patients with functional nausea.

ACKNOWLEDGMENTS

The efforts of Dr. Xu were supported in part by a grant from the American College of Gastroenterology.

COMMENTS

Nausea is a common and debilitating symptom complaint. In many patients the underlying pathophysiology is unknown and likely represents a combination of gastric pathophysiology and psychological issues. There are few medications available, many of which have significant side effects. The traditional approach of acupuncture allows several likely underlying conditions to be treated at the same time.

Research frontiers

While acupuncture has been studied in treatment of nausea of chemotherapy, postoperatively and during pregnancy, no studies have been published on its use in functional nausea. Most published studies also use acupuncture and one site, which is a different approach to the general clinical acupuncture approach. Based on experience and the finding that 14/22 subjects had documented history of depression, a holistic approach which treated multiple clinical conditions was used. The same acupuncture points were used in all patients.

Innovations and breakthroughs

The study showed a significant improvement in degree of nausea in subjects who presented with moderate/severe nausea. The degree of nausea improved over the three treatment visits suggesting a lasting effect. Both bloating and pain were improved by acute treatment with acupuncture, but it is unclear whether the pre-treatment VAS score accurately reflects the severity of chronic complaints by the patients. The main innovation in this study was the holistic approach to treat both gastrointestinal and psychological conditions concurrently.

Applications

Data from this study would support the need for a controlled study to examine the effect of treatment and to control for factors such as concurrent psychological conditions and belief in acupuncture as a treatment.

Terminology

Functional nausea-symptom of nausea in the absence of anatomic or biochemical abnormalities, such as pregnancy, ulcer disease, obstruction *etc.* Dyspepsia-chronic upper abdominal pain. The symptom may be associated with ulcer, but functional dyspepsia is a condition with similar symptoms but in the absence of identifiable pathology in the stomach.

Peer review

It is an interesting paper integrating Traditional Chinese Medicine (acupuncture) with Western Medicine. The author has included a lot of thought provoking factors in this paper, such as the causes of nausea, the Chinese medical theory of imbalance, the conducted placebo controlled studies failed to show a difference compared to sham treatment, activation of brain region related to needle stimulation, and that acupuncture affected the response, and so on.

REFERENCES

- 1 Talley NJ, Locke GR, Lahr BD, Zinsmeister AR, Tougas G, Ligozio G, Rojavin MA, Tack J. Functional dyspepsia, delayed gastric emptying, and impaired quality of life. *Gut* 2006; **55**: 933-939
- 2 Strömberg AS, Sjogren P, Goldschmidt D, Petersen MA, Pedersen L, Groenvold M. Symptom priority and course of symptomatology in specialized palliative care. *J Pain Symptom Manage* 2006; **31**: 199-206
- 3 Tack J, Talley NJ, Camilleri M, Holtmann G, Hu P, Malagelada JR, Stanghellini V. Functional gastroduodenal disorders. *Gastroenterology* 2006; **130**: 1466-1479
- 4 Nowak TV, Johnson CP, Kalbfleisch JH, Roza AM, Wood CM, Weisbruch JP, Soergel KH. Highly variable gastric emptying in patients with insulin dependent diabetes mellitus. *Gut* 1995; **37**: 23-29
- 5 Kim Y, Morrow GR. Changes in family relationships affect the development of chemotherapy-related nausea symptoms. *Support Care Cancer* 2003; **11**: 171-177
- 6 Chen XN. Chinese Acupuncture and Moxibustion. Beijing: Foreign Languages Press, 1999: 200-201, 416-420, 430-431
- 7 Kaptchuk TJ. Acupuncture: theory, efficacy, and practice. *Ann Intern Med* 2002; **136**: 374-383
- 8 Ezzo J, Vickers A, Richardson MA, Allen C, Dibble SL, Issell B, Lao L, Pearl M, Ramirez G, Roscoe JA, Shen J, Shivan J, Streitberger K, Treish I, Zhang G. Acupuncture-point stimulation for chemotherapy-induced nausea and vomiting. *J Clin Oncol* 2005; **23**: 7188-7198
- 9 Alkaiissi A, Evertsson K, Johnsson VA, Ofenbartl L, Kalman S. P6 acupressure may relieve nausea and vomiting after gynecological surgery: an effectiveness study in 410 women. *Can J Anaesth* 2002; **49**: 1034-1039
- 10 Koch KL, Hong SP, Xu L. Reproducibility of gastric myoelectrical activity and the water load test in patients with dysmotility-like dyspepsia symptoms and in control subjects. *J Clin Gastroenterol* 2000; **31**: 125-129
- 11 Chang CS, Ko CW, Wu CY, Chen GH. Effect of electrical stimulation on acupuncture points in diabetic patients with gastric dysrhythmia: a pilot study. *Digestion* 2001; **64**: 184-190
- 12 Belluomini J, Litt RC, Lee KA, Katz M. Acupressure for nausea and vomiting of pregnancy: a randomized, blinded study. *Obstet Gynecol* 1994; **84**: 245-248
- 13 Norheim AJ, Pedersen EJ, Fønnebø V, Berge L. Acupressure treatment of morning sickness in pregnancy. A randomised, double-blind, placebo-controlled study. *Scand J Prim Health Care* 2001; **19**: 43-47
- 14 Jewell D, Young G. Interventions for nausea and vomiting in early pregnancy. *Cochrane Database Syst Rev* 2003: CD000145
- 15 Vickers AJ. Statistical reanalysis of four recent randomized trials of acupuncture for pain using analysis of covariance. *Clin J Pain* 2004; **20**: 319-323
- 16 Hu S, Stritzel R, Chandler A, Stern RM. P6 acupressure

- reduces symptoms ofvection-induced motion sickness. *Aviat Space Environ Med* 1995; **66**: 631-634
- 17 **Yoo SS**, Teh EK, Blinder RA, Jolesz FA. Modulation of cerebellar activities by acupuncture stimulation: evidence from fMRI study. *Neuroimage* 2004; **22**: 932-940
- 18 **Ouyang H**, Yin J, Wang Z, Pasricha PJ, Chen JD. Electroacupuncture accelerates gastric emptying in association with changes in vagal activity. *Am J Physiol Gastrointest Liver Physiol* 2002; **282**: G390-G396
- 19 **Tatewaki M**, Strickland C, Fukuda H, Tsuchida D, Hoshino E, Pappas TN, Takahashi T. Effects of acupuncture on vasopressin-induced emesis in conscious dogs. *Am J Physiol Regul Integr Comp Physiol* 2005; **288**: R401-R408
- 20 **Tatewaki M**, Harris M, Uemura K, Ueno T, Hoshino E, Shiotani A, Pappas TN, Takahashi T. Dual effects of acupuncture on gastric motility in conscious rats. *Am J Physiol Regul Integr Comp Physiol* 2003; **285**: R862-R872
- 21 **Pariente J**, White P, Frackowiak RS, Lewith G. Expectancy and belief modulate the neuronal substrates of pain treated by acupuncture. *Neuroimage* 2005; **25**: 1161-1167

S- Editor Liu Y **L- Editor** Roberts SE **E- Editor** Li JL