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Clinical Study

Efficacy observation on acupuncture for diabetic gastroparesis

针刺治疗糖尿病胃轻瘫的临床疗效观察

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Abstract

Objective: To observe the effect of acupuncture on gastric motility, plasma motilin and serum gastrin in patients with diabetic gastroparesis (DGP) and evaluate its clinical efficacy.

Methods: A total of 100 eligible cases were randomly allocated into an acupuncture group (n=50) and a control group (n=50). Patients in the acupuncture group were treated by needling Zhongwan (CV 12), Zusanli (ST 36) and Neiguan (PC 6), whereas patients in the control group were treated with oral administration of Domperidone. The clinical efficacies of the two groups were compared; and changes in gastric motility, plasma motilin and serum gastrin in both groups were observed before and after treatment.

Results: After treatment, the symptom scores, gastric motility and contents of plasma motilin and serum gastrin were significantly improved in both groups (P<0.05). There were between-group statistically significant differences in symptom scores, gastric motility and levels of plasma motilin and serum gastrin after treatment (all P<0.05). The total effective rate was 96% in the treatment group, versus 78% in the control group, showing a statistically significant difference (P<0.05).

Conclusion: Acupuncture is effective for DGP and can reduce the levels of plasma motilin and serum gastrin.

Keywords: Acupuncture Therapy; Diabetes Mellitus, Type 2; Gastroparesis; Point, Zhongwan (CV 12); Point, Zusanli (ST 36); Point, Neiguan (PC 6)

【摘要】目的：观察针刺疗法对糖尿病胃轻瘫患者胃动力、血浆胃动素和血清胃泌素的影响，评价其临床疗效。**方法：**将 100 例符合纳入标准的患者随机分为针刺组和对照组，每组各 50 例。观察组取中脘、足三里和内关针刺治疗，对照组给予多潘立酮治疗。观察两组临床疗效及治疗前后胃动力、血浆胃动素、血清胃泌素的变化。**结果：**治疗后,两组总体症状积分、胃动力及血浆胃动素、血清胃泌素水平与同组治疗前比较，差异均有统计学意义(均 P<0.05)；治疗后，观察组总体症状积分、胃动力及血浆胃动素、血清胃泌素水平与对照组比较，差异均有统计学意义(P<0.05)；观察组总有效率为 96%，对照组为 78%，两组比较差异具有统计学意义(P<0.05)。**结论：**针刺对糖尿病胃轻瘫有一定临床疗效,可降低血浆胃动素、血清胃泌素水平。

【关键词】针刺疗法; 2 型糖尿病; 胃轻瘫; 穴,中脘; 穴, 足三里; 穴, 内关
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Diabetic gastroparesis (DGP) is a common complication of long-standing diabetes mellitus. It is characterized by the stomach taking too long to empty its contents without mechanical obstruction. Patients may present with early feeling of fullness after eating, lack of appetite, nausea, vomiting and abdominal bloating. This condition can severely affect the patients' quality of life and result in erratic blood glucose levels and in turn make diabetes worse. In modern medicine, DGP is mainly addressed with prokinetic (promotility) agents. However, these agents can cause toxic or adverse reactions if taken for a long period of time. So far there are no ideal therapeutic drugs for this condition[1]. This randomized controlled clinical trial aimed to observe the clinical effect of acupuncture on DGP and investigate its action mechanism. The results are now summarized as follows.

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1 Clinical Data

1.1 Diagnostic criteria

1.1.1 Diagnostic criteria in Western medicine

This was based on the diagnostic criteria in Guidelines for Prevention and Treatment of Type-2 Diabetes (2010 edition) stipulated by Chinese Medical Association[2]: having diabetes for at least 5 years; abdominal bloating, early satiety, lack of appetite, nausea and vomiting with presence or absence of

gastroliths; gastroscopy shows normal liver function and no gastric mucosa damage or pyloric obstruction; having complications of peripheral neuropathy or diabetic retinopathy; and X-ray examination shows radiopaque markers 4 hours after eating.

1.1.2 Diagnostic criteria in Chinese medicine

This was based on the Criteria for Deficiency Syndrome Differentiation in Chinese Medicine stipulated in National Academic Conference on Deficiency in Chinese and Western Medicine and Geriatric Studies in 1986[3].

Major symptoms: A poor appetite, general fatigue, abdominal bloating after eating or in the afternoon, and abnormal bowel movements (loose stools or alternating hard and loose stools).

Adjunct symptoms: Mental fatigue, reluctance to talk, tastelessness, no thirst, dull lingering abdominal pain, nausea, vomiting, gastric stuffiness, bowel sounds, a sallow complexion, edema and weakness in passing stools. The tongue is pale swollen with teeth marks and a thin white coating. The pulse is thready and weak.

The diagnosis can be made on the basis of 2 major symptoms or one major symptom coupled with one adjunct symptom.

1.2 Inclusion criteria

Those who met the diagnostic criteria for type-2 diabetes, DGP and spleen deficiency in Chinese medicine; fasting blood glucose reading ≤7.0 mmol/L and blood glucose reading 2 h after eating ≤10 mmol/L; aged older than 30 with no gender limitation; signed the informed consent and were willing to participate in the trial.

1.3 Exclusion criteria

Having organic digestive tract disorders; having severe diarrhea, abnormal liver functions or diabetic ketoacidosis; having unclear or complicated syndromes; a history of abdominal surgery; having severe primary diseases in cardiovascular, liver, kidney and hemopoietic systems; having severe neurosis or menopausal syndrome; those allergic to agents used in this trial; pregnant (including women ready to be pregnant) or breast-feeding women.

1.4 Statistical method

The SPSS 13.0 version software was used for statistical analysis. The *t*-test was used for measurement data, which was expressed as mean ± standard deviation ($\bar{x} \pm s$). The Chi-square test was used for enumeration data. A *P* value of less than 0.05 indicated a statistical significance.

1.5 General materials

A total of 100 outpatients treated in our department between December 2011 and March 2014 agreed to participate in this trial. They were randomly allocated into an acupuncture group (n=50) and a control group (n=50). The acupuncture group included 26 males and 24 females, aged between 40 and 65 (mean age: 58) and their disease duration lasted from 5 to 12 years (mean duration: 8 years). The control group included 27 males and 23 females, aged between 42 and 63 (mean age: 58.5) and their disease duration lasted from 5 to 13 years (mean duration: 8.2 years). There were no between-group statistically significant differences in comparing gender composition, age and duration (all $P > 0.05$), indicating that the two groups were comparable (Table 1).

Table 1. Between-group comparison of baseline data

Group	n	Gender (case)		Mean age ($\bar{x} \pm s$, year)	Mean duration ($\bar{x} \pm s$, year)
		Male	Female		
Acupuncture	50	26	24	58.0±7.5	8.0±3.7
Control	50	27	23	58.5±5.7	8.2±4.6

2 Treatment Methods

A week prior to the trial, patients in both groups discontinued medications that may affect digestive tract motility, such as anticholinergics, proton pump inhibitors, antiemetic and prostaglandin, etc. The blood glucose was well controlled through education on diabetes mellitus, diet, and oral antidiabetic drugs or insulin.

2.1 Acupuncture group

Point: Zhongwan (CV 12), bilateral Zusanli (ST 36) and Neiguan (PC 6).

Method: The patient took a supine lying position. After routine sterilization, the above points were punctured perpendicularly using disposable filiform needles (0.30 mm in diameter and 40 mm in length), 30 mm for Zhongwan (CV 12) and Zusanli (ST 36), and 25 mm for Neiguan (PC 6), followed by 30 s twirling manipulation (rotating amplitude: 360°; frequency: 100 times/min) upon arrival of qi. The manipulation was done once every 5 min. The needles were retained for 30 min.

The acupuncture treatment was performed once a day and there was a 2-day interval after 5 d. Four weeks made up a course of treatment.

2.2 Control group

Patients in the control group took 10 mg Domperidone (Motilium, 10 mg/tablet, manufactured by Xi'an Janssen Pharmaceutical Ltd., China) 30 min before meals for each dose, 3 doses a day, for a total of 4 weeks.

3 Therapeutic Efficacy Results

3.1 Observation items

3.1.1 Symptom scores

The symptom score sheet was based on the clinical

symptom grading and quantifying standard in the *Guiding Principles for Clinical Study of New Chinese Medicines*[4]: 3 points for severe symptoms; 2 points for moderate symptoms, 1 point for mild symptoms, and 0 point for no symptoms. The symptom scores in the two groups were evaluated before and after treatment (Table 2).

Table 2. Symptom score sheet

Symptom	Score		
	Severe (3 points)	Moderate (2 points)	Mild (1 point)
Abdominal bloating	Severe bloating that lasts at least 2 h, affects life and doesn't respond well to symptomatic drugs	Abdominal bloating/fullness that lasts 0.5-1 h, affects life to some degree or needs to be addressed by symptomatic drugs	Mild bloating that alleviates or disappears within 0.5 h without symptomatic drugs and doesn't affect life
Nausea/vomiting	Frequent nausea with vomiting or urges to vomit	Occasional nausea with urges to vomit	Occasional nausea
Poor appetite/early satiety	Food amount reduced by more than 2/3	Lack of appetite, foot amount reduced by1/3	Lack of appetite, food amount remain unchanged
General fatigue	Fatigue with an inability to maintain daily activities	Fatigue but can still manage to maintain daily activities	Mild fatigue and can maintain mild physical exertion

3.1.2 Stomach emptying test

The stomach emptying test was conducted prior to treatment. All patients discontinued prokinetic agents one week before the test.

Method: A day before the test, the patient stopped eating after 19:00 and stopped drinking after 24:00. At 8:00 am on the day of the test, the patient ate 80 g instant noodles with 200 mL boiled water mixed with 20 barium strips (1 mm × 10 mm, 10 mg/strip, manufactured by the Institute of Aerospace Medicine) and 50 g ham sausage within 5 min. After eating, the patient could stand, walk and sit but not lie down. Then 4 h later, an X-ray machine (model: 1000MA, manufactured by Siemens Co., Ltd., German) was used to detect the residual barium strips. The DGP diagnosis can be made in case of presence of ≥3 residual barium strips. Four weeks after treatment, the above method was used again for gastric emptying test.

3.1.3 Measurement of plasma motilin and serum gastrin concentrations

Radioimmunoassay was used to measure the plasma motilin and serum gastrin concentrations respectively before treatment and 4 weeks after treatment.

Method: After 12 h fasting of food and water, 10 mL venous blood of the patients were drawn in the morning next day and placed into a tube containing 30 μL 10% EDTA solution and 30 μL aprotinin solution, immediately followed by centrifugation (speed: 3 500 r/min; temperature: 4 ℃). Then the isolated plasma was put into a −30 ℃ refrigerator, for radioimmunoassay. The MTL Elisa kits and 131I-labeled gastrin radioimmunoassay kits were provided by Beijing North Institute of Biological Technology (China).

3.2 Therapeutics efficacy criteria

The efficacy criteria were based on the *Guiding Principles for Clinical Study of New Chinese Medicines*[4]. The symptom scores were evaluated and recorded for calculation of symptom improvement rate.

The improvement rate = (Pre-treatment score − Post-treatment score) ÷ Pre-treatment score × 100%.

Recovery: Improvement rate ≥75%.

Marked effect: Improvement rate ≥50%, <75%.

Improvement: Improvement rate ≥25%, <50%.

Failure: Improvement rate <25%.

3.3 Treatment results

3.3.1 Between-group comparison in symptom scores, gastric emptying, plasma motilin and serum gastrin

It can be seen from Table 3 that before treatment, there were no between-group statistical differences in comparing symptom scores, gastric emptying, plasma motilin, and serum gastrin ($P>0.05$); after treatment, there were significant intra-group differences in all items in the acupuncture group ($P<0.05$) as well as significant between-group differences in all items ($P<0.05$), indicating a better effect in improving the gastric motility and gastrointestinal hormones in the acupuncture group than in the control group.

3.3.2 Between-group comparison in clinical efficacy

It can be seen from table 4 that the total effective rate was 96% in the acupuncture group, versus 78% in the control group, showing a statistical significance ($P < 0.05$) and indicating a better efficacy in the acupuncture group than in the control group.

Table 3. Between-group comparisons in symptom scores, stomach emptying, plasma motilin and serum gastrin ($\bar{x}$ ±*s*)

Item	Acupuncture group (*n*=50)		Control group (*n*=50)	
	Before treatment	After treatment	Before treatment	After treatment
Symptoms scores (point)	9.96±1.03	1.28±0.61[1)2)]	9.87±1.25	4.58±0.21
Residual barium strips	7.85±1.17	2.01±1.02[1)2)]	7.69±1.25	4.83±1.37
Gastrin (ng/L)	151.67±20.02	101.87±16.15[1)2)]	153.09±18.35	137.97±17.56
Motilin (ng/L)	410.57±16.98	187.03±16.07[1)2)]	408.73±17.56	287.67±21.07

Note: Intra-group comparison before and after treatment, 1) $P<0.05$; compared with the control group, 2) $P<0.05$

Table 4. Between-group comparison in clinical efficacy

Group	*n*	Recovery	Marked effect	Improvement	Failure	Total effective rate (%)
Acupuncture	50	25	18	5	2	96.0[1)]
Control	50	17	17	5	11	78.0

Note: Compared with the control group, 1) $P<0.05$

4 Discussion

DGP is a common and chronic complication of diabetes mellitus. It is a sign of autonomic neuropathy and characterized by low gastric motility and delayed gastric emptying. Patients may experience nausea, vomiting, early satiety and prolonged postprandial fullness and bloating[5].

The gastrointestinal hormones constitute a group of hormones secreted by enteroendocrine cells. Gastrin is a peptide hormone released by G cells in the pyloric antrum of the stomach, duodenum, and the pancreas. Normally, it stimulates secretion of gastric acid, enhances the activity of the pyloric pump and moderately increases gastric motility. However, high gastrin may inhibit gastric motility. Motilin (MTL) is a polypeptide hormone secreted by endocrine M cells that are numerous in crypts of the small intestine. Its major function is to increase the migrating myoelectric complex component of gastrointestinal motility. Russo A, *et al* found that patients with diabetes mellitus have compensatory elevation of gastrin; however, their interdigestive myoelectric complex (DMEC) III-related activities diminished or disappeared, resulting in disturbed gastric motility and delayed emptying[6]. The majority of scholars have reported a higher plasma MTL level in DGP patients than in normal healthy people[7-8].

In Chinese medicine, DGP falls under the category of 'stuffiness or fullness'. The underlying cause is disordered qi ascending and descending due to spleen qi deficiency. Factors affecting the descending of stomach qi include qi stagnation, blood mass, dampness, turbid-phlegm, food retention, and damp-heat. The treatment strategies are to strengthen the spleen, harmonize the stomach and down-regulate stomach qi[9-13]. Zhongwan (CV 12) is an influential point of the Fu organs and the Front-Mu point of the stomach. It acts to harmonize the stomach and resolve stomach fullness or stuffiness. Zusanli (ST 36) is the He-Sea of the Stomach Meridian and the Lower He-Sea point of the stomach. It acts to circulate qi, strengthen the spleen, harmonize the stomach, generate qi and blood, increase gastrointestinal motility and thus alleviate symptoms of DGP. Neiguan (PC 6) acts to regulate qi activities, soothe the chest and down-regulate stomach qi. Studies have shown that needling Zusanli (ST 36) can increase the gastric electrical activity in patients with spleen deficiency[14]. Huang YX, *et al* have found that needling Zusanli (ST 36) can significantly increase gastric motility in rats[15]. Xu JJ, *et al* have found that needling Zusanli (ST 36) can regulate gastric electrical wave and enhance gastric motility in functional dyspepsia (FD) rats[16]. Takahashi T has reported that needling Zusanli (ST 36) can increase muscle contraction and gastric motility through parasympathetic pathways; and needling Zhongwan (CV 12) can relax muscle and inhibit secretion of gastric acid[17]. Peng SF, *et al* have reported that electric stimulation on Neiguan (PC 6) and Zusanli (ST 36) can significantly alleviate the symptoms of FD patients, improve their mental state and effectively enhance their gastric electrical activities and vagus nerve functions[18].

According to the findings of this clinical trial, the clinical symptoms, gastrointestinal motility and gastrointestinal hormones in the acupuncture group were more significantly improved than those in the control group ($P<0.05$), indicating that acupuncture has an exact effect for DGP. The action mechanism might be related to its functions in lowering motilin and gastrin levels and increasing gastrointestinal motilities. This method is convenient, economical and has fewer side effects as well as better patient compliance.

Conflict of Interest

The authors declared that there was no conflict of interest in this article.

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Statement of Informed Consent

Informed consent was obtained from all individual participants included in this study.

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