

# A Selective Effect of Combined Treatment of Electroacupuncture at *Zusanli*(ST36), Manual Acupuncture, and *Pyengwi-san* in Function Dyspepsia Patients with Pyloric Valve Disturbance and Hypoactivity of Gastric Vagus Nerve

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### ABSTRACT

**Objectives** : The aim of this study was to evaluate the therapeutic effect of acupuncture and herbal medicine in patients who had hypoactivity of the gastric vagus nerve and pyloric valve disturbance simultaneously with function dyspepsia by bowel sounds analysis.

**Methods** : Bowel sounds of 10 patients (male 1, female 9) were recorded and their % of bowel sound (%BS) and ratio of dominant frequency (DF) were analyzed before and after treatment. Hypoactivity of the gastric vagus nerve was considered if % BS was <6%, and pyloric valve disturbance was accepted if DF ratio (e.g., postprandial DF/fasting DF) was <1. Electroacupuncture at *Zusanli* (ST36, 3Hz, 30 minutes) and manual acupuncture at other meridian points were applied daily for 2 weeks. Herbal medicine, *Pyengwi-san*, was administered to all patients (100cc, 3 times/day).

**Results** : DF ratio significantly increased from  $0.93 \pm 0.06$  to  $1.06 \pm 0.04$  after treatment for 2 weeks ( $p=0.005$ ). 9 of 10 patients were improved to DF ratio >1. %BS also increased from  $2.97 \pm 1.17\%$  to  $4.49 \pm 4.27\%$ , not significantly. 3 patients showed a remarkable elevation, and their %BS reached >6% of normal value.

**Conclusions** : Combined effect of electroacupuncture at *Zusanli* (ST36), manual acupuncture, and *Pyengwi-san* was shown effective in the improvement of pyloric valve disturbance more than hypoactivity of gastric vagus nerve on patients with functional dyspepsia.

**Key words** : Electroacupuncture, *Zusanli*(ST36), Bowel Sound, Vagus nerve, Pyloric valve, Functional Dyspepsia.

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## I. 緒論

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Functional dyspepsia is a functional syndrome, which is diagnosed in the absence of underlying organic disease that readily explains the symptoms<sup>1</sup>.

There have been many oriental medical studies including etiology, differential diagnosis, and treatments about it. Especially therapeutic effect of herbal medicine or acupuncture in the clinical studies was reported respectively<sup>2-4</sup>. But real practice in clinical field has preferred these therapies as a form of combination, because their synergetic effect was expected in treating this disease.

We reported recently that a combined therapy containing electrical stimulation of *Zusanli*(ST36), manual acupuncture at other meridian points, and *Pyengwis*an produced the bidirectional effect on the vagus nerve activity and pyloric valve function in patients with functional dyspepsia<sup>5</sup>. Their vagus nerve activity and pyloric valve function were generally improved, but sometimes aggravated from normal to abnormal level. Thus, for further clarifying its effect on them, it is needed to investigate selectively patients who complicated hypoactivity of gastric vagus nerve and pyloric valve disturbance simultaneously.

The purpose of present study was to confirm which of gastric vagal activity and pyloric valve function is better in the therapeutic effect.

## II. Methods

### 1. Subjects

10 patients with both hypoactivity of gastric vagus nerve and pyloric valve disturbance in analysis of bowel sounds were choosed through chart-review among 49 patients diagnosed and treated with functional dyspepsia at the Oriental Gastroenterology Clinic at the ○○University

Oriental Medical Hospital from 1/1, 2007 to 9/30, 2008. Patients were predominantly female(1 male and 9 female), and mean age of them was  $40.7 \pm 18.0$  years.

All of the subjects had no evidence of organic disease(including endoscopy findings) that could explain the symptoms, no evidence that the dyspeptic symptom was eased after defecation or was related with a change in the consistence of the stool, and no history of other medication and abdominal surgery.

### 2. Method

#### 1) Treatment

##### (1) Electroacupuncture

Everyday both *Zusanli*(ST36) points were stimulated twice by electroacupuncture apparatus (ITO, PG-6, Japan) at 1p.m. and 7p.m. for 2 weeks(3Hz, 30minutes). Stimulation intensity was 1.2 times of the pain threshold in the acupoints.

##### (2) Manual Acupuncture

Lingdao(HT4), Shenmen(HT7), Sangwan(CV13), Zhongwan(CV12), Xiawan(CV10), *Zusanli*(ST36), and Taichong(LR3) were manually stimulated by acupuncture needle(Haeng Lim Seo Won Acu Needle Co., stainless steel, diameter 0.25mm, length 40mm) for 30 minutes at 9:30.

##### (3) Herbal Medicine

One pack of *Pyengwis*an (code number HK228 on the prescribing book of Kyunghee oriental medical center) was boiled with water and administered to all patients for general digestives (100cc, 3 times/day). The composition of the prescription is described in Table 1.

Table 1. Contents of Pyengwisan

Herb	Drug Name	Scientific Name	Dose(g)
蒼朮	Atractylodis Rhizoma	Atractylodes japonica Koidzumi	8g
陳皮	Citri Pericarpium	Citrus nobilis Makino	5g
厚朴	Magnoliae Cortex	Magnolia officinalis REHD. Et WILS	4g
甘草	Glycyrrhizae Radix	Glycyrrhiza uralensis FISCH	2g
Total Amount			19g

## 2) Measurement of Gastric Vagal Activity and Pyloric Valve Function

Activity of gastric vagus nerve and pyloric valve function were assessed by analyzing bowel sounds. Activity of gastric vagus nerve was expressed as Percentage of Bowel Sound(%BS), pyloric valve function as Dominant Frequency (DF, Hz) ratio(eg, postprandial DF/fasting DF).

Recording of bowel sounds was done in a quiet and slightly dark room, and patients lay supine except when they eat a test meal(two pieces of toast, two broiled eggs, and orange juice 180ml, total 480Kcal), To reduce a motion artifact, patients was cautioned not to move unnecessarily, talk, breath deeply, and sleep.

Bowel sounds were recorded from the patient who had fasted overnight. Fasting sample of 15 minutes and postprandial sample of 40 minutes after eating a test meal for 10 minutes were obtained.

Bowel sounds were recorded and analyzed by following procedures. Electric stethoscope ES-120 (Jac Instrument, Van Nuys, CA, USA) was attached to right lower quadrant abdomen. Analogue signals of electric stethoscope were transferred to digital recorder(Voice of VTR, Voice it Worldwide, Inc; sampling 8000Hz), and recording data were delivered to IBM computer via converter. %BS(%) and DF(Hz) was calculated by EnteroTach bowel sound analysis

software(ver 4.0 Western Researchs, Tuscon, AZ, USA).

## 3) Protocol and Evaluation

(1) Recording of bowel sounds was performed twice before and after treatment for 2 weeks.

(2) Hypoactivity of gastric vagus nerve was considered if %BS was <6%, and pyloric valve disturbance was accepted if DF ratio was <1<sup>6</sup>.

(3) The therapeutic effect of this therapy was evaluated retrospectively. Data are expressed as the mean  $\pm$  standard deviation. Wilcoxon signed rank test was used when comparing changes of %BS and DF ratio before and after treatment. A *p* value of <.05was regarded as significant.

## III. Results

Part showing a significant therapeutic effect with this treatment was the pyloric valve function, not gastric vagal activity(Table 2). DF ratio significantly increased from  $0.93 \pm 0.06$  to  $1.06 \pm 0.04$  after treatment for 2 week( $p=0.005$ ). 9 of 10 patients were improved to DF ratio>1(Fig. 1).

%BS also increased from  $2.97 \pm 1.17\%$  to  $4.49 \pm 4.27\%$ , it was not significant. However, 3 patients showed a remarkable elevation, and their %BS reached >6% of normal value(Fig. 2). One of them showed only an improvement in %BS, but not in DF ratio.

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Table 2. The Characteristics of Patients and Changes of %of Bowel Sounds and Dominant Frequency Ratio after Treatment.

Patients Number	Sex	Age	% of Bowel Sounds		Dominant Frequency Ratio	
			Before	After	Before	After
1	F	20	1.41	0.15	0.94	<b>1.15</b>
2	F	24	1.44	3.77	0.98	<b>1.07</b>
3	F	33	1.82	2.52	1.00	<b>1.02</b>
4	F	43	2.71	2.48	0.92	<b>1.06</b>
5	F	65	2.76	2.90	0.88	<b>1.04</b>
6	F	58	3.12	3.14	0.96	<b>1.07</b>
7	F	49	3.58	1.98	0.98	<b>1.05</b>
8	M	16	3.72	<b>9.72</b>	0.96	<b>1.07</b>
9	F	35	4.4	<b>9.75</b>	0.78	0.99
10	F	64	4.76	<b>13.07</b>	0.92	<b>1.09</b>
Mean±S.D.		40.7±18.0	2.97±1.17	4.49±4.27	0.93±0.06	1.06±0.04
P-value			0.169		0.005*	

\*. P<0.05, Wilcoxon signed rank test

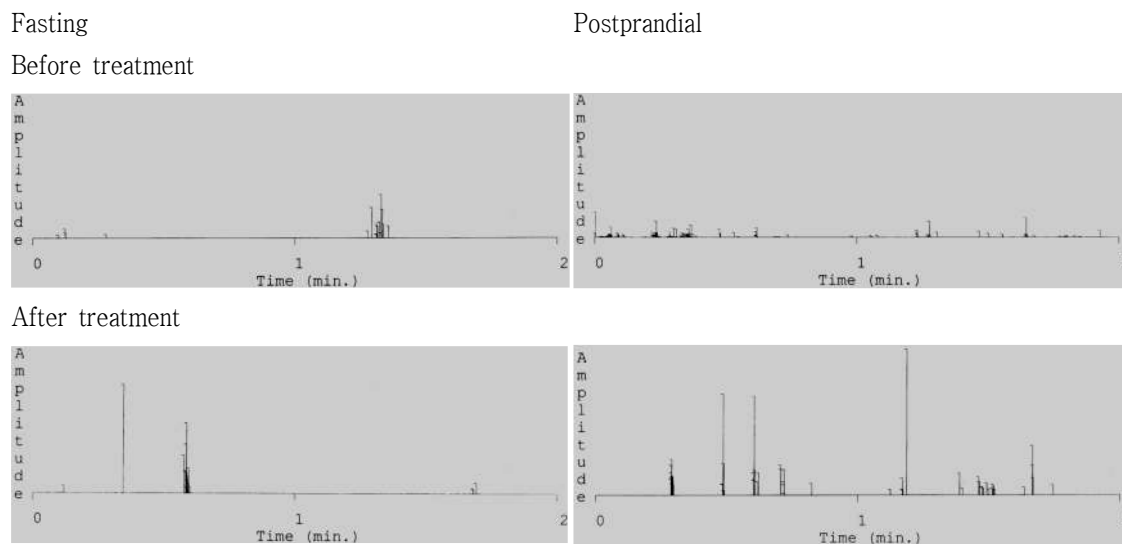


Fig. 1 The Recording of Patient Number 1. After treatment, bowel sounds in fasting and post prandial showed higher amplitudes than before. In this case, Dominant Frequency ratio(DF) improved to DF>1. However, % of Bowel Sound was much decreased than before.

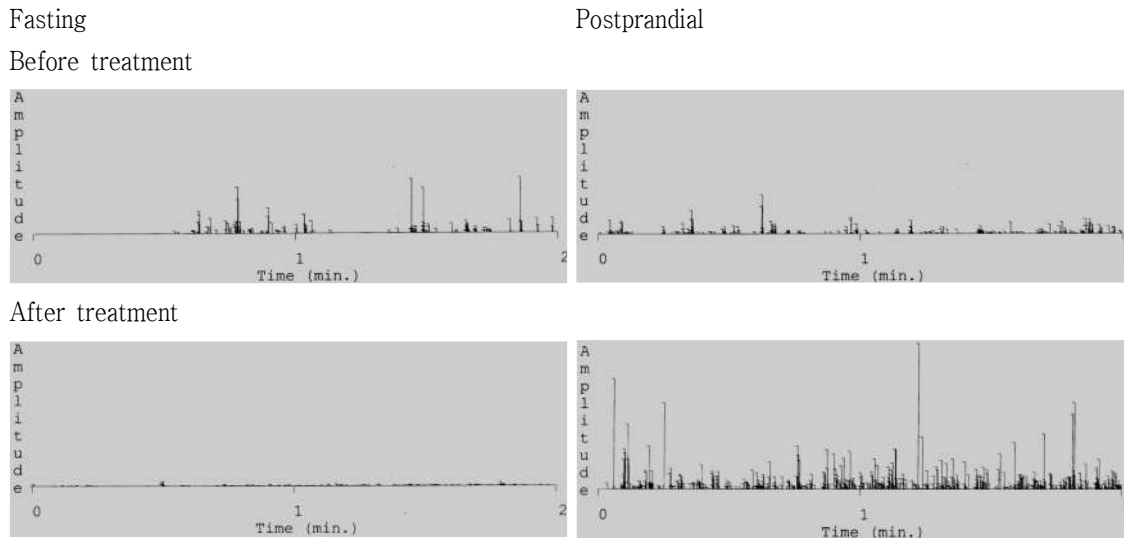


Fig. 2 The Recording of Patient Number 10. After treatment, amplitudes and frequency in fasting bowel sounds were lower and decreased than before treatment. However, postprandial sounds showed higher amplitude and increased frequency than before. % of Bowel Sound and Dominant Frequency ratio improved to  $\%BS>6$  and  $DF>1$  respectively.

#### IV. Discussion

The result of this study was shown that a combined therapeutic effect of Zusalni(ST36) electroacupuncture, manual acupuncture, and Pyengwisan was better in pyloric valve function than gastric vagal activity. Bowel sound test was useful as a tool examining pyloric valve function and gastric vagal activity in these patients.

Cannon<sup>7</sup> wrote the first systematic report about abdominal auscultation in relation to the structure and function of the stomach and intestines in 1905. Hence, the interest in abdominal auscultation had decreased with time, and there have been only some reports that bowel sounds is decreased or increased in patients with such disorders as appendicitis, mechanical obstruction, and paralytic ileus<sup>8</sup>. Because hearing sensation level of human has a limitation, abdominal auscultation was

considered just as a traditional technique. However, with the increasing use of computers it has been possible to begin to analyze bowel sounds in a quantitative manner. So diagnosis and assessment by using bowel sounds recently come into spotlight in the clinical practice.

The difficulties in analyzing bowel sounds are what the origin of sounds is and what effects the change of sounds. Because abdominal auscultation test records the sound obtained from the whole abdomen, it is difficult to locate the exact source of the sound. But it is generally accepted that stomach is the most important site. Politzer<sup>9</sup> concluded that bowel sound is influenced by viscus content and production of bowel sounds is the most active in the stomach. Yamaguchi<sup>10</sup> monitoring simultaneously the motility of the antrum of the stomach by ultrasonography, reported that the abdominal sound auscultated immediately after

food intake was the gastroduodenal sound. Craine<sup>11</sup> calculated the position of each bowel sound based on a triangulation algorithm using the sound envelope intensity as measured from each of the three stethoscopes, and founded that the majority of sounds mapped to the stomach area in the patients with nonulcer dyspepsia.

The prime requisite for the production of a sound wave is a vibrating object and a transmitting medium<sup>12</sup>. So pyloric valve is considered as the most characteristic source of sound. Craine<sup>11</sup> suggested that the transition valves from one part of the gastrointestinal tract to the next may generate the majority of bowel sounds. Tomomasa<sup>13,14</sup> showed that the amount of gastrointestinal sound was decreased in patient with pyloric stenosis before surgery and increased after pyloromyotomy, and suggested that gastrointestinal sounds is increased when antrum contracts and supplies gas into the intestine. Yamaguchi<sup>10</sup> also suggested that gastroduodenal sound was considered as a sound that occurred in association with stomach emptying.

Therefore, we previously reported that pyloric valve disturbance may be one of the causes of postprandial epigastric fullness in functional dyspepsia by analyzing bowel sounds and it was related to Domain Frequency(DF) ratio<sup>6</sup>. Anticholinergic agent decreases the amount of abdominal sounds<sup>15</sup>, so percentage of bowel sounds(%BS) can be considered as the outcome of gastric vagal effect. According to this, we examined patients who have hypoactivity of gastric vagus nerve(%BS<6) and pyloric valve disturbance(DF ratio<1) simultaneously, which compared with data of normal bowel sounds in healthy control<sup>6</sup>.

Kim<sup>5</sup> already reported the effect of acupuncture on gastric vagus nerve activity and pyloric valve

function in patients with function dyspepsia. But the previous study didn't include patients who had both disorders at the same time. Hence the rate of these patients was estimated only 11% among patients who visited our clinic with functional dyspepsia<sup>16</sup>, it was difficult to collect and evaluate them. Therefore, there was a limitation of recruiting patients by considering sufficient numbers and sexual distribution.

In the previous study, it was reported that total cure rate of hypoactivity of vagus nerve is 16% and that of pyloric valve disturbance is 37%. And the aggravation of pyloric valve function shifting from normal to abnormal level was higher than that of %BS<sup>5</sup>. Present study also showed that it was easier to recover to normal level in DF ratio than in %BS.

The cause of low %BS has still unknown. On the grounds that 50% of patients with low %BS had a family history<sup>16</sup>, it seems quite probable that low %BS is related to genetic factor<sup>17, 18</sup>. And considering that number of females with low %BS was three times more than that of male<sup>16</sup>, it may be also related to gender difference. Recently it was reported in Japan that the genetic factor (COX-1 gene) was significantly associated with the development of epigastric pain syndrome subgroup of functional dyspepsia in female subjects<sup>19</sup>. On the other hand, the percentage of family history in patients with pyloric valve disturbance was 25%, and sex ratio was 1:1<sup>16</sup>. Therefore, it may be caused by external factors unlike hypoactivity of gastric vagus nerve. This reason may explain why the therapeutic effect of this treatment showed better in pyloric valve disturbance than in hypoactivity of gastric vagus nerve in present study.

The mechanisms of acupuncture on gastric motility are still unclear. When the abdomen(ex.

Zhongwan, CV12) was stimulated by acupuncture, gastric motilities were inhibited as a result of increased activity of the efferent fibers of the gastric sympathetic nerves<sup>20,21</sup>. Increased gastric motilities after acupuncture stimulations to limbs (ex. *Zusanli*, ST36) were resulted from increased activity of the efferent fibers of the gastric vagus nerves<sup>20,21</sup>. However, interaction between reflex facilitation and inhibition of gastric motility during simultaneous stimulation of both limbs and abdomen was observed as partial cancellation of each effect by the other<sup>22</sup>. But sympathetic reflex inhibition of gastric motility seemed to be much stronger than the vagal reflex facilitatory effect<sup>22</sup>. Therefore, it seems that manual acupuncture inhibited gastric motility and reducing pain through sympathetic nerve.

It is generally known that the effect of electroacupuncture at *Zusanli*(ST36) is facilitating gastric motility through gastric vagus nerve. But *Zusanli* point may have dual effect on the regulation of the pylorus peristaltic function<sup>23</sup>. Especially variation of electrical vagal stimulus frequency altered the response from excitation of pyloric contraction(0.2–0.5Hz) to inhibition at higher ones(>0.7Hz), suggesting that both the excitatory and inhibitory vagal pathways are present<sup>24</sup>. Therefore, therapeutic effect of acupuncture may vary depending on not only the different acupoints but also the frequency and intensity of stimulation.

Herbal medicine, Pyengwisan was equally administered to all patients as general digestives, and it was proved experimentally that Pyengwisan has no effect on gastric motility<sup>25</sup>. Therefore, role of herbal medicine, Pyengwisan, wasn't regarded as prokinetic drug importantly in this study. But the possibility that different gastrointestinal effect of

Pyengwisan affected on the current result still remains.

Patients with both hypoactivity of gastric vagus nerve and pyloric valve disturbance were known to complain of dyspeptic symptoms most severely among groups of dyspeptic patients<sup>16</sup>, and pyloric valve disturbance was considered as the cause of postprandial epigastric fullness<sup>6</sup>. However, the change of symptoms weren't described in this study. Most of all, a treatment focusing on pyloric valve function may be strategically advantageous in the improvement of gastric motility or relief of dyspeptic symptoms. In addition, it is necessary to enhance vagal activity by modifying acupuncture technique, which is related with gastric contraction, for the more relief of symptoms in these patients.

In this study, patients who were the upper 3 in %BS before treatment were improved to normal level of %BS(3.72→9.72, 4.40→9.75, 4.76→13.07%). And a patient who had the lowest DF ratio before treatment couldn't be improved to normal level(0.78→0.99). From this phenomenon, it is thought that if a certain degree of vagus nerve activity is maintained, normal vagus nerve activity can be restored by this treatment. It would be needed to examine what a threshold level is. We hope an active try to improve the gastric vagal activity for patients with gastric dysmotility related to vagus neuron.

## Conclusion

The combined treatment of electroacupuncture at *Zusanli*(ST36), manual acupuncture, and Pyengwisan improved more effectively pyloric valve disturbance than hypoactivity of gastric vagus nerve in patients with functional dyspepsia.

## 한방치료가 위 미주신경 활성 저하와 유문부 기능 장애가 병발된 기능성 소화불량증 환자에 미치는 선택적 효능

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### ABSTRACT

**목적** : 위 미주신경 활성 저하와 유문부 기능 장애를 동시에 가지고 있는 기능성 소화불량증 환자에서 전침 및 한약의 복합치료 치료가 이 두가지 면에서 각각 어떤 영향을 미치는지를 살펴보았다.

**방법** : 장음검사상 위 미주신경 활성 저하와 유문부 기능 장애를 동시에 가지고 있는 환자 10명을 대상으로 치료 전후의 장음 지표 변화를 비교하였다. 장음지표는 % of bowel sound (%BS)와 주 주파수(dominant frequency, DF)를 사용하였으며, %BS<6인 경우를 위 미주신경 활성저하 DF ratio(식후/식전)<1를 유문부 기능장애로 평가하였다. 환자들에게 2주간 족삼리전침과 체침이 매일 시술되었으며 평위산 전탕액이 하루 3회 투여되었다.

**결과** : 2주간의 치료 후 DF ratio는  $0.93 \pm 0.06$ 에서  $1.06 \pm 0.04$ 로 유의성있게 증가했으며, 10명 중 9명의 환자가 DF ratio>1의 정상치로 회복되었다. %BS 역시  $2.97 \pm 1.17\%$ 에서 4.27%로 증가했지만 통계적 유의성은 없었으며, 3명의 환자에서 %BS가 6이상으로 정상회복되었다.

**결론** : 위 미주신경 활성 저하와 유문부 기능 장애를 동시에 가지고 있는 기능성 소화불량증 환자에 대한 족삼리 전침과 일반 체침, 평위산의 치료는 미주신경 활성 저하보다는 유문부 기능 장애에 더 유의한 효과를 보였다.

**Key words** : 족삼리전침, 장음, 미주신경, 유문부 기능, 기능성 소화불량증

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