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Clinical Study

Acupuncture with Du's heat-reinforcing method for diarrhea-predominant irritable bowel syndrome: a randomized controlled trial

"杜氏热补法"针刺治疗腹泻型肠易激综合征：随机对照研究

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Abstract

Objective: To compare the clinical efficacy of Du's heat-reinforcing method and Western medication in treating diarrhea-predominant irritable bowel syndrome (IBS-D).

Methods: Sixty-five IBS-D patients were randomized into two groups by the random number table. Thirty-three cases in the treatment group were intervened by acupuncture with Du's heat-reinforcing method, while thirty-two cases in the control group were given oral administration of pinaverium bromide tablets. The intervention lasted 4 weeks for both groups. The IBS symptom severity score (IBS-SSS), IBS-quality of life (IBS-QOL) and hospital anxiety and depression scale (HAD) were adopted to evaluate the therapeutic efficacy.

Results: The two groups each had two dropout cases. The clinical recovery rate was 38.7% and the total effective rate was 90.3% in the treatment group versus 13.3% and 66.7% in the control group. The treatment group was superior to the control group in both clinical recovery rate and total effective rate (both $P<0.05$). After 1-week and 4-week treatment, respectively, the IBS-SSS scores were lower compared with the baseline in both groups, and the intra-group differences were statistically significant (both $P<0.05$); the score in the treatment group was lower than that in the control group, and the between-group difference was statistically significant (both $P<0.05$). After 4-week treatment, the component scores of IBS-QOL showed improvements in both groups, and the treatment group was superior to the control group in the improvements of dysphoria, interference with activity, health worry and food avoidance (all $P<0.05$). The anxiety and depression scales of HAD (HAD-a, HAD-d) in the treatment group and the HAD-a in the control group obtained significant improvements (all $P<0.05$); the scores of HAD-a and HAD-d in the treatment group were significantly better than those in the control group (both $P<0.05$).

Conclusion: Acupuncture with Du's heat-reinforcing method can effectively ease the symptoms of IBS-D, improve the quality of life and the state of anxiety and depression. It can produce a more significant efficacy than oral administration of pinaverium bromide tablets.

Keywords: Acupuncture Therapy; Acupuncture Reinforcing Method; Irritable Bowel Syndrome; Diarrhea; Randomized Controlled Trial; Du Xiao-shan

【摘要】目的：比较"杜氏热补法"与西药治疗腹泻型肠易激综合征(IBS-D)的临床疗效。**方法：**将65例IBS-D患者按随机数字表法随机分为2组，治疗组33例采用"杜氏热补法"针刺治疗，对照组32例口服匹维溴铵片治疗。两组均治疗4周。通过肠易激综合征症状严重度评分(IBS-SSS)、肠易激综合征生活质量评分(IBS-QOL)、医院焦虑抑郁量表(HAD)评定两组疗效。**结果：**治疗组脱落2例，对照组脱落2例。治疗组临床治愈率38.7%，总有效率90.3%；对照组临床治愈率13.3%，总有效率66.7%。治疗组的临床治愈率及总有效率均优于对照组(均$P<0.05$)。治疗1周和4周后，两组IBS-SSS评分均低于治疗前，组内差异具有统计学意义(均$P<0.05$)；治疗组评分低于对照组，组间差异具有统计学意义(均$P<0.05$)。治疗4周后，两组IBS-QOL各项评分均改善，治疗组在改善烦躁不安、冲突行为、健康忧虑、饮食限制方面优于对照组(均$P<0.05$)；治疗组HAD中焦虑子量表(HAD-a)和抑郁子量表(HAD-d)，以及对照组的HAD-a评分均有改善(均$P<0.05$)；治疗组HAD-a和HAD-d评分均优于对照组(均$P<0.05$)。**结论：**"杜氏热补法"针刺可有效缓解IBS-D患者临床症状，提高患者生活质量，改善患者焦虑、抑郁状态，疗效优于口服匹维溴铵片。

【关键词】针刺疗法；针刺补法；肠易激综合征；腹泻；随机对照试验；杜晓山

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Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by abdominal pain or discomfort coupled with altered bowel habits and/or abnormal stool pattern, but without responsible morphological or biochemical changes. IBS is a common disease and affects 10.0%-15.0% of the world's population[1]. In China, the incidence rate of IBS is 4.6%-5.7%[2]. It has been classified into four types, i.e. diarrhea-predominant IBS (IBS-D), constipation-predominant IBS (IBS-C), mixed type (alternating constipation and diarrhea) of IBS (IBS-M) and unspecified type of IBS (IBS-U). Among which, IBS-D is the most common one[3]. Patients with IBS-D usually suffer from frequent defecation, uncontrollable urge to defecate and abdominal discomfort, which will undermine the patients' quality of life (QOL), or even result in mental disorders, such as anxiety and depression. To seek an effective acupuncture-moxibustion treatment paradigm for IBS-D, we designed this randomized controlled clinical trial. The aim was to observe the efficacy of acupuncture with Du's heat-reinforcing method in treating IBS-D, and its influence on the patient's mental state, with oral administration of pinaverium bromide tablets as the control. The report is given as follows.

1 Clinical Materials

1.1 Diagnostic criteria

The diagnosis was in accordance with the diagnostic criteria of IBS in Roman Ⅲ criteria[4]. Recurrent abdominal pain or discomfort for at least 3 d in the last 3 months, coupled with 2 or more of the following symptoms: ① symptoms were released after defecation; ② change in defecation frequency; ③ alteration in form (appearance) of stool. The symptoms occurred at least 6 months before the diagnosis, without morphological or biochemical evidence, and the manifestations in the previous 3 month conformed to the above diagnostic criteria. IBS-D meant that loose or water-like stool occurred in ≥25% of the defecation, while hard and dry stool happened in <25% of the defecation.

1.2 Inclusion criteria

Conformed to the above diagnostic criteria of IBS-D[4-5]; aged 18-65 years old; disease duration over 6 months; the IBS symptom severity score (BIS-SSS) ≥75 points at the baseline[6]; not taking any medication specifically for IBS-D in the past 2 weeks; not receiving acupuncture-moxibustion treatment for IBS-D in the previous 3 months; willing to participate in the trial and having signed the informed consent form; able to comprehend the scales adopted in this trial.

1.3 Exclusion criteria

Those with organic intestinal disorders or diseases that may affect the digestive function (such as diabetes and thyroid dysfunction); those on long-term use of medications for promoting gastrointestinal motility or regulating intestinal function; with a history of abdominal or anorectal surgery; simultaneously using other treatments or medications; accompanied by severe primary diseases involving respiratory, digestive or cardio-cerebrovascular systems; pregnant or breast-feeding women; allergic constitution; allergic to metal or feared of needles; participating in other studies at the same time.

1.4 Dropout criteria

Those with poor compliance or quitted halfway, or the medical data were incomplete; those who were unable to accept acupuncture treatment; those with severe adverse events or complications occurred during the study.

1.5 Statistical methods

The SPSS version 22.0 statistical software was used for statistical analysis. The measurement data with normal distribution and homogeneity of variance were expressed as mean ± standard deviation ($\overline{x} \pm s$). For these data, independent samples *t*-test was used in between-group comparisons and paired *t*-test was used in intra-group comparisons. For measurement data with heterogeneity of variance, *t*'-test was used. The measurement data not in normal distribution were analyzed by Chi-square test. The ranked enumeration data were examined by non-parametric test. $P<0.05$ was considered to be statistically significant.

1.6 General data

This trial had been approved by the Ethics Committee of Wuxi Hospital of Traditional Chinese Medicine (No. 2015NL-030-02). A total of 65 IBS-D patients were recruited during April 2016 and July 2017 from the Acupuncture-moxibustion Department of Wuxi Hospital of Traditional Chinese Medicine. They were randomized into a treatment group of 33 cases and a control group of 32 cases by the random number table at a ratio of 1:1. During the study, 2 cases in the treatment group dropped out (1 case quitted due to personal affairs; the other for the fear of needles); 2 cases dropped out in the control group (one for taking other medications without permission; the other was unable to complete the intervention due to work). The flow of the trial is shown in Figure 1. Finally, 61 IBS-D patients finished the intervention, 31 in the treatment group and 30 in the control group. There were no significant differences in the data of gender, age or disease duration between the two groups (all $P>0.05$), indicating the comparability (Table 1).

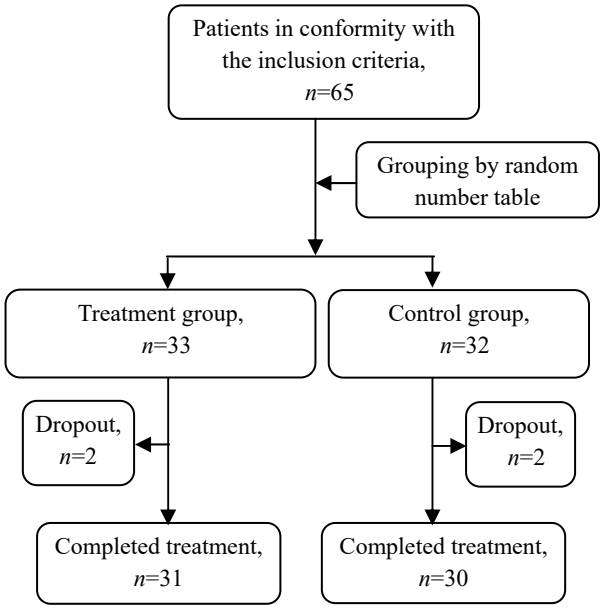

Figure 1. The flow chart of the study

Table 1. Comparison of the general data

Group	*n*	Gender (case)		Average age ($\bar{x}$ ±*s*, year)	Average duration ($\bar{x}$ ±*s*, month)
		Male	Female		
Treatment	31	21	10	39.5±2.1	71.0±8.4
Control	30	19	11	39.9±2.1	69.4±7.6

2 Treatment Methods

2.1 Treatment group

Acupoints: Guanyuan (CV 4) and bilateral Neiguan (PC 6), Zusanli (ST 36), Sanyinjiao (SP 6), Tianshu (ST 25) and Shangjuxu (ST 37).

Method: The patient took a supine position. After standard sterilization for the doctor's hands and the to-be-treated acupoints, disposable filiform needles of 0.30 mm in diameter and 40 mm in length were used for acupuncture. Upon the arrival of needling qi, corresponding manipulations were performed. Du's heat-reinforcing method was applied to Zusanli (ST 36) and Tianshu (ST 25). To perform this manipulation, the needles were inserted deeper for another 0.1-0.2 cun after the arrival of needling qi with repeated forceful-thrusting and gentle-lifting performance. Afterwards, the doctor twisted the needle in one direction by moving the thumb forward and index finger backward. During this process, the doctor had to ensure the maintenance of needling sensations, which meant that he should always feel a heavy, tight or unsmooth sensation with the needle, until the patient felt warm-hot in the operated area or in the lower belly. The manipulation could be performed multiple times to guarantee the ideal effect. The rest acupoints were treated with even reinforcing-reducing manipulations and the needles were manipulated once every 10 min after the needling qi was obtained. The needles were retained 30 min for each session, and the treatment was performed once every other day, 3 times a week, for a total of 4 weeks (12 sessions).

To guarantee the therapeutic efficacy, the acupuncture treatment was conducted by the doctor who is the successor of 'Du's acupuncture manipulations' and has had over 10 years of clinical experience.

2.2 Control group

Patients in the control group were intervened by oral administration of pinaverium bromide tablets (dicetel, Abbott Laboratories Trading Co., Ltd.), 50 mg each time, 3 times a day, taken with meal, for a total of 4 weeks. The tablets should be swallowed, not broken, melted or chewed.

After 4-week treatment, the therapeutic efficacy was evaluated by a researcher who was not involved in grouping and treatment.

3 Observation of Therapeutic Efficacy

3.1 Observation items

3.1.1 IBS-SSS

IBS-SSS consists of 5 dimensions including the duration of abdominal pain, severity of abdominal pain, abdominal bloating, bowel habit dissatisfaction and life interference. Each dimension ranges from 0 to 100 and the full score is 500 points. A score <75 points, remission stage; 75-174 points, mild; 175-299 points, moderate; ≥300 points, severe. The evaluation of IBS-SSS was performed prior to the treatment and after 1-week and 4-week treatment, respectively.

3.1.2 IBS-quality of life (IBS-QOL)

The purpose of IBS-QOL is to measure the QOL among IBS-D patients[7]. This scale has 34 items which measure 8 dimensions, i.e. dysphoria, interference with activity, body image, health worry, food avoidance, social reaction, sexual and relationships. Each item is measured by a 5-point response scale: not at all, slightly, moderately, quite a bit and a great deal, respectively scoring 5, 4, 3, 2 and 1. The higher the score, the better the QOL. This scale was evaluated at the first visit and after 4-week treatment.

3.1.3 Hospital anxiety and depression scale (HAD)

HAD consists of two subscales, which are HAD-anxiety scale (HAD-a) and HAD-depression scale (HAD-d)[8]. Each item on the scale is scored 0-3. A total score of 0-7 stood for no depression/anxiety; 8-10 points, borderline abnormal; 11-20 points, abnormal. This scale was evaluated at the first visit and after 4-week treatment.

3.2 Criteria of therapeutic efficacy

The therapeutic efficacy was determined based on the result of IBS-SSS[9].

Clinical recovery: The total score of IBS-SSS <75 points.

Markedly effective: The total score of IBS-SSS was improved by two levels.

Effective: The total score of IBS-SSS was improved by one level.

Invalid: The total score of IBS-SSS showed no improvement or got worse.

The above scales were evaluated by a researcher who had no access to the information of grouping and treatment, and this researcher was also in charge of data analyses after the intervention.

3.3 Treatment results

3.3.1 Comparison of clinical efficacy

After 4-week treatment, the clinical recovery rate was 38.7% and the total effective rate was 90.3% in the treatment group, versus 13.3% and 66.7% in the control group. The clinical recovery rate and total effective rate of the treatment group were significantly higher than those of the control group (both $P<0.05$), (Table 2).

3.3.2 Comparison of the IBS-SSS score

There was no significant difference in the IBS-SSS score between the two groups before the intervention ($P>0.05$), indicating the comparability. Compared with the baseline, the IBS-SSS scores were improved significantly in both groups respectively after 1-week and 4-week treatment (all $P<0.05$), suggesting that the two methods both can mitigate the symptoms of IBS-D. Compared with the score after 1-week treatment, the IBS-SSS score showed significant improvement in the treatment group after 4-week treatment ($P<0.05$), while the improvement at the same time point was insignificant in the control group ($P>0.05$). Respectively after 1-week and 4-week treatment, the decrease in the IBS-SSS score was more significant in the treatment group compared with the control group at the same time point ($P<0.05$), indicating that the treatment group was superior to the control group in the improvement of IBS-SSS score after 1-week and 4-week treatment, respectively (Table 3).

Table 2. Comparison of the clinical efficacy (case)

Group	*n*	Clinical recovery	Markedly effective	Effective	Invalid	Clinical recovery rate (%)	Total effective rate (%)
Treatment	31	12	9	7	3	38.7[1)]	90.3[1)]
Control	30	4	8	8	10	13.3	66.7

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

Table 3. Comparison of the IBS-SSS score ($\bar{x}\pm s$, point)

Group	*n*	Pre-treatment	After 1-week treatment	After 4-week treatment
Treatment	31	281.77±12.49	222.41±11.92[1)3)]	100.97±8.55[1)2)3)]
Control	30	289.83±11.58	260.83±10.38[1)]	254.17±11.98[1)]

Note: Compared with the baseline in the same group, 1) $P<0.05$; compared with the score after 1-week treatment in the same group, 2) $P<0.05$; compared with the control group at the same time point, 3) $P<0.05$

3.3.3 Comparison of the IBS-QOL score

There were no significant differences in the component scores of IBS-QOL between the two groups before the intervention (all $P>0.05$), indicating the comparability. Compared with the baseline, the IBS-QOL component scores were significantly improved in both groups after 4-week treatment (all $P<0.05$), suggesting that the two methods both can effectively improve the QOL of the IBS-D patients. After 4-week treatment, the scores of dysphoria, interference with activity, health worry and food avoidance achieved more significant improvements in the treatment group compared with those in the control group (all $P<0.05$), while the between-group differences in the rest dimensions of the scale were statistically insignificant (all $P>0.05$). The results showed that the treatment group was better than the control group in improving dysphoria, interference with activity, health worry and food avoidance after 4-week treatment, while the effects on the other items were equivalent between the two groups (Table 4).

3.3.4 Comparison of the HAD score

There were no significant differences in the scores of HAD-a and HAD-d between the two groups before the treatment (both $P>0.05$), suggesting the comparability. Compared with the baseline, the scores of HAD-a and HAD-d showed significant improvements in the treatment group after 4-week treatment (both $P<0.05$); in the control group, the HAD-a score was significantly improved after 4-week treatment ($P<0.05$) but the improvement in the HAD-d score was insignificant ($P>0.05$). After 4-week treatment, the improvements in

the HAD-a and HAD-d scores were more significant in the treatment group than in the control group (both $P<0.05$), suggesting that the treatment group had more significant improvements in the anxiety and depression state compared with the control group after 4-week treatment (Table 5).

Table 4. Comparison of the IBS-QOL score ($\bar{x}$ ±s, point)

Item	Treatment group (n=31)		Control group (n=30)	
	Pre-treatment	After 4-week treatment	Pre-treatment	After 4-week treatment
Dysphoria	69.96±1.96	87.20±1.58[1)2)]	69.90±3.13	79.59±2.56[1)]
Interference with activity	29.26±2.74	67.86±2.21[1)2)]	30.24±2.71	54.17±2.85[1)]
Body image	38.31±2.87	66.53±2.42[1)]	41.88±3.51	64.17±3.78[1)]
Health worry	61.29±3.31	84.41±2.31[1)2)]	59.17±3.28	72.50±2.97[1)]
Food avoidance	22.04±2.46	70.43±2.96[1)2)]	23.33±3.13	55.83±3.07[1)]
Social reaction	39.31±2.68	66.33±2.71[1)]	38.33±3.32	61.88±3.12[1)]
Sexual	28.63±2.91	59.68±2.30[1)]	29.58±3.14	59.17±2.47[1)]
Relationships	43.01±4.84	65.59±2.30[1)]	43.06±4.50	62.50±3.59[1)]

Note: Compared with the baseline in the same group, 1) $P<0.05$; compared with the control group at the same time point, 2) $P<0.05$

Table 5. Comparison of the HAD score ($\bar{x}$ ±s, point)

Group	n	HAD-a		HAD-d	
		Pre-treatment	After 4-week treatment	Pre-treatment	After 4-week treatment
Treatment	31	12.29±0.69	7.06±0.50[1)2)]	11.06±0.55	6.29±0.42[1)2)]
Control	30	12.23±0.60	9.87±0.51[1)]	11.03±0.59	10.43±0.49

Note: Compared with the baseline in the same group, 1) $P<0.05$; compared with the control group at the same time point, 2) $P<0.05$

4 Discussion

IBS-D patients mainly experience diarrhea with abdominal pain, often accompanied by autonomic nerve disorders such as irritation, insomnia, vertigo, anxiety and depression. Psychological factor plays a significant role in the development of this medical issue. According to its main manifestations, IBS-D belongs to the scope of abdominal pain or diarrhea in traditional Chinese medicine (TCM). TCM holds that this disorder is majorly associated with emotional problems, attack of external pathogens and internal damages caused by improper diet, which may cause qi stagnation, dysfunction of spleen-stomach in transporting and transforming, and abnormal movement of large intestine. The heart, liver and spleen are majorly affected while the kidney may be affected in the long run.

The pathogenesis and etiology of IBS-D are unclear. However, with the development of neurogastroenterology and on-going research in molecular biology, the brain-gut axis disorder caused by chronic psychological disorders is believed to be closely related to the onset of IBS-D. It's found that IBS-D patients tend to develop a vicious cycle or dysfunction of brain-gut axis[10]. The dysfunction of brain-gut axis led by chronic psychological disorders will then increase the reaction of IBS-D patients to stresses, resulting in visceral hypersensitivity. The pathological and physiological mechanisms of IBS-D share the brain-gut axis as a common path[11-13]. The intestinal nervous system communicates with the central nervous system by releasing neurotransmitters, forming up a neuroendocrine network. The body uses this network for bi-directional regulation. Stimulatory signals such as anxiety and depression affect gastrointestinal motility and the relevant hormone levels via this network. Meanwhile, abnormal secretion of gastrointestinal hormones will also work on the central nervous system, aggravating the psychological disorders such as anxiety and depression[14-15]. Acupuncture-moxibustion can modulate the brain-gut peptide[16] towards a normal state. Through either a general (brain-gut axis) or a local (gastrointestinal tract) regulation, it can regulate yin-yang, qi, blood and Zang-fu organs in the body[17-18].

As an intangible culture heritage of Wuxi City, Jiangsu Province of China, 'Du's acupuncture manipulations' are easy for patients to accept because it merely causes pain, and it is free of toxic or side effects and the therapeutic efficacy is satisfactory. It's found through clinical experience that one of Du's acupuncture

manipulations, Du's heat-reinforcing method, can produce significant efficacy in the treatment of IBS-D. A study reported that when Shao Shan Huo (mountain-burning fire) manipulation was applied to Zusanli (ST 36), the patient felt a warm- hot feeling occurred and the electrogastrogram (EEG) presented both excitation and inhibition; when the warm-hot feeling disappeared, the effect of acupuncture on EEG still existed, suggesting that the Shao Shan Huo (mountain-burning fire) manipulation can produce a lasting excitation effect on stomach[19]. Du's heat-reinforcing manipulation originated from Shao Shan Huo (mountain-burning fire) manipulation[20]. Mr. Du Xiao-shan holds that obtaining needling qi sensations should be the premise and holding qi sensation should be the key to the success of this acupuncture manipulation, and conducting qi sensation to the affected area along the meridians is an important way to enhance the therapeutic efficacy. Therefore, the heavy-thrusting and gentle-lifting performance should be repeated without a fixed number of times and insertion depth, which makes it easier to perform but the efficacy more significant.

The current study showed that Du's heat-reinforcing method and Western medication both were effective for IBS-D. However, after 4-week treatment (12 sessions), compared with oral administration of pinaverium bromide tablets, Du's heat-reinforcing method produced a faster effect in releasing IBS-D symptoms and the effect was enhanced with the length of the treatment. At the end of the 4-week intervention, Du's heat-reinforcing method was superior to pinaverium bromide tablets in improving dysphoria, interference with activity, health worry and food avoidance; but the two methods were equivalent in improving body image, social reaction, sexual and relationships. Besides, at the end of the 4-week intervention, Du's heat-reinforcing acupuncture method showed a better effect in ameliorating the anxiety and depression state of the IBS-D patients, better than oral administration of pinaverium bromide tablets. Du's heat-reinforcing acupuncture method also produced higher clinical recovery rate and total effective rate than orally taking pinaverium bromide tablets in treating IBS-D.

To conclude, Du's heat-reinforcing acupuncture method not only can ease the IBS-D symptoms, but also improve the anxiety and depression state and the QOL, showing that acupuncture-moxibustion can produce a multi-target, bi-directional and multi-path regulation effect to treat diseases[21], and is worth promoting in clinical practice.

Conflict of Interest

The authors declared that there was no potential 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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