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Clinical Study

Acupuncture treatment for depressive symptom in diarrhea-predominant irritable bowel syndrome: a randomized controlled study

针刺治疗腹泻型肠易激综合征抑郁症状的随机对照研究

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Abstract
Objective: To observe the clinical efficacy of acupuncture treatment for depressive symptom in diarrhea-predominant irritable bowel syndrome (IBS-D).
Methods: A total of 70 patients with IBS-D accompanied by depressive symptom were randomized into a control group and an observation group, with 35 cases in each group. The control group was treated with oral intake of pinaverium bromide tablets, and the observation group was treated with regulating liver and spleen acupuncture treatment. The two groups were treated for 4 weeks. The scores of IBS symptom severity scale (IBS-SSS) and self-rating depression scale (SDS) were assessed before and after treatment.
Results: After treatment, there were statistical significant differences in the scores of abdominal pain degree, abdominal pain frequency and defecation satisfaction level and the total score between the two groups (all $P<0.05$). The SDS score of the observation group was obviously decreased, and the improvement was significantly superior to that in the control group ($P<0.05$).
Conclusion: Acupuncture treatment can significantly improve gastrointestinal symptom and depressive symptom in patients with IBS-D.
Keywords: Acupuncture Therapy; Acupuncture-moxibustion Therapy; Irritable Bowel Syndrome; Diarrhea; Depression

【摘要】目的：观察针刺治疗腹泻型肠易激综合征抑郁症状的临床疗效。**方法：**将70例腹泻型肠易激综合征伴抑郁症状的患者随机分为对照组和观察组，每组35例。对照组给予匹维溴铵片口服，观察组给予调肝脾针刺治疗。两组均治疗4周。治疗前及治疗后评定肠易激综合征症状严重程度量表(IBS-SSS)及抑郁自评量表(SDS)。**结果：**治疗后，两组腹痛程度、腹痛频率、排便满意度的评分及总分的差异均有统计学意义(均$P<0.05$)；观察组的SDS评分明显降低，且改善程度明显优于对照组($P<0.05$)。**结论：**针刺能显著改善腹泻型肠易激综合征患者的胃肠道症状及抑郁症状。

【关键词】针刺疗法；针灸疗法；肠易激综合征；腹泻；抑郁
【中图分类号】R246.1　　**【文献标志码】**A

Irritable bowel syndrome (IBS) is a common functional bowel disease, with abdominal pain, abdominal distension and changes in bowel habits and stool form as the main clinical manifestations[1]. The disease is mainly divided into 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)[2]. The incidence of IBS is high, and about 7%-21% of the populations meet the diagnostic criteria of IBS[3]. IBS patients often present with depressive symptom. It is found that the incidence of depression in IBS patients is 37.1%, and IBS coupled with depressive symptom often means a poor prognosis[4]. Western medicine mainly uses symptomatic treatments such as antispasmodic drugs, antidiarrheal or laxative drugs, intestinal microecologics, antidepressant and anti-anxiety drugs, while the clinical efficacy is uncertain[5]. As a green therapy, acupuncture can effectively release IBS and depressive symptom, and has certain advantages[6-8]. Therefore, in this study, we applied acupuncture therapy to regulate liver and spleen for depressive symptom of IBS-D, and compared it with pinaverium bromide tablets.

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1 Clinical Materials

1.1 Diagnostic criteria

1.1.1 Diagnostic criteria of Western medicine

This study referred to the diagnostic criteria of IBS-D in *Rome* Ⅳ[9]. The disease duration is over 6 months. Repeated abdominal pain has occurred in the past 3 months, with at least one attack in a week, and with at least 2 of the following items at the same time: ① abdominal pain associated with defecation; ② attacks accompanied by changes in defecation frequency; ③ attacks accompanied by changes in stool form. The IBS-D type is: mushy stool or watery stool ≥25%, hard stool <25%.

1.1.2 Diagnostic criteria of Chinese medicine

Diagnostic criteria of liver qi stagnation and spleen deficiency syndrome referred to the *Guiding Principles for Clinical Research of New Drugs in Traditional Chinese Medicine*[10]: diarrhea, occurred or aggravated due to abnormal emotions, symptoms released after diarrhea; emotional depression or irritability; loss of appetite, fatigue; a pale tongue, a stringy and thready pulse or a stringy and slippery pulse.

1.2 Inclusion criteria

Those aged 18 to 60 years old; met the diagnostic criteria of IBS-D of Western medicine; met the diagnostic criteria of syndrome of liver qi stagnation and spleen deficiency; the score of self-rating depression scale (SDS) ≥50 points; agreed to participate in this trial and signed informed consent.

1.3 Exclusion criteria

Those with severe cardiovascular, lung, kidney or systemic diseases; pregnant or breast-feeding women; those who participated in other clinical trial at the same time; those who took medicines that might affect gastrointestinal function in the past 3 months.

1.4 Shedding criteria

Those who dropped out during treatment; those presented severe adverse reactions during the trial; those got worse in condition of the disease.

1.5 Statistical methods

All data were statistically analyzed by SPSS version 20.0 statistical software. The comparison of counting data was processed by Chi-square test. Rank-sum test was applied for the comparison of ranked data. Measurement data were expressed as mean ± standard deviation ($\bar{x} \pm s$), and matched samples *t*-test was applied for the intra-group comparison before and after treatment. Group *t*-test was applied for the comparison between the groups. $P<0.05$ was considered to indicate a statistically significant difference.

1.6 General data

A total of 70 patients with IBS-D accompanied by depressive symptom were selected from our hospital between August 2016 and August 2018. All patients were randomly divided into an observation group and a control group by the simple random number table method, with 35 cases in each group. There were no dropout cases during the observation. There were no statistically significant differences in the general data such as gender, age and duration of disease between the two groups (all $P>0.05$), indicating that they were comparable (Table 1).

Table 1. Comparison of general data between the two groups

Group	*n*	Gender (case)		Average age ($\bar{x} \pm s$, year)	Average duration ($\bar{x} \pm s$, month)
		Male	Female		
Observation	35	16	19	39.3±11.5	25.9±12.0
Control	35	13	22	38.4±13.5	26.0±12.9

2 Treatment Methods

2.1 Observation group

The observation group received acupuncture treatment.

Acupoints: Taichong (LR 3), Zusanli (ST 36), Shangjuxu (ST 37), Sanyinjiao (SP 6), Tianshu (ST 25), Baihui (GV 20) and Yintang (GV 29).

Methods: The patient took a supine position. After the routine disinfection of fingers and acupoints, the physician punctured the acupoints using Hwato brand sterile acupuncture needles of 0.33 mm in diameter and 40 mm in length (Suzhou Medical Supplies Factory Co., Ltd., China). Then the physician subcutaneously punctured Baihui (GV 20) by 15-20 mm in depth; obliquely punctured Yintang (GV 29) downwards by 10-15 mm in depth with skin-pinching up needle insertion method; perpendicularly punctured Tianshu (ST 25), Zusanli (ST 36), Shangjuxu (ST 37), Sanyinjiao (SP 6) and Taichong (LR 3) by 15-25 mm in depth. After th insertion, twirling manipulation was applied slowly and continuously at a small range to give the patient a persistent, gentle and comfortable needling sensation. The needle manipulation for each acupoint was performed 2-3 min. The needles were retained for 30 min and the needle manipulation was performed twice during the retention. The treatment was performed 5 times a week, for 4 weeks in total.

2.2 Control group

Oral intake of pinaverium bromide tablet (Dicetel®, Abbott Healthcare SAS, France, national drug registration number: H20120127), 50 mg per dose, 3 times a day, for 4 weeks in total.

3 Observation of Curative Efficacy

3.1 Observation items

3.1.1 IBS symptom severity scale (IBS-SSS)[11-12]

The total scores of IBS-SSS of the two groups before

and after treatment were compared. IBS-SSS consists of five parts: degree of abdominal pain, frequency of abdominal pain, degree of abdominal distension, defecation satisfaction and life interference. The scoring range of each part is 0-100 points, and the total score of IBS-SSS is 500 points. The higher the score, the severer the symptoms of IBS.

3.1.2 Self-rating depression scale (SDS)[13-14]

The scores of SDS of both groups before and after treatment were compared. SDS contains a total of 20 questions, each with a score of 1-4 points. The sum of the scores of the 20 questions is the rough score, which then multiplies by 1.25. And the integer part of this result is the standard score. The higher the score, the severer the symptoms. The cut off value for depression is 50 points.

3.2 Criteria of curative efficacy

According to the nimodipine method, the criteria of curative effect were established with SDS reduction rate.

SDS reduction rate = (SDS score before treatment – SDS score after treatment) ÷ SDS score before treatment × 100%.

Cured: Clinical symptoms basically disappeared, and SDS reduction rate ≥90%.

Marked effect: Clinical symptoms obviously improved, and SDS reduction rate ≥60%, but <90%.

Effective: Clinical symptoms improved, and SDS reduction rate ≥30%, but <60%.

Invalid: No improvements in clinical symptoms, or even worse, and SDS reduction rate <30%.

3.3 Results

3.3.1 Comparison of curative efficacy

The total effective rate was 94.3% in the observation group, significantly higher than 65.7% in the control group (P<0.05), (Table 2).

3.3.2 Comparison of the IBS-SSS score

There were no significant differences in each item score and total score of IBS-SSS between the two groups before treatment (all P>0.05). After treatment, the scores of the degree of abdominal pain, the degree of abdominal distension and the total score in the control group decreased significantly (all P<0.05). The changes in scores of the frequency of abdominal pain, defecation satisfaction and life interference were not statistically significant (all P>0.05). In the observation group, the scores of the degree of abdominal pain, the frequency of abdominal pain, the degree of abdominal distension, defecation satisfaction and life interference and the total score were significantly decreased after treatment (all P<0.05). After treatment, the scores of the degree of abdominal pain, the frequency of abdominal pain and defecation satisfaction, and the total score in the observation group were lower than those in the control group, and the differences were statistically significant (all P<0.05). There were no significant differences in the scores of the degree of abdominal distension and life interference between the two groups (all P>0.05), (Table 3).

Table 2. Comparison of curative efficacy between the two groups (case)

Group	n	Cured	Marked effect	Effective	Invalid	Total effective rate (%)
Observation	35	8	12	13	2	94.3[1)]
Control	35	1	5	17	12	65.7

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

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

Group	n	Time	Degree of abdominal pain	Frequency of abdominal pain	Degree of abdominal distension	Defecation satisfaction	Life interference	Total score
Observation	35	BT	59.43±29.70	60.57±29.70	65.14±29.64	56.00±31.73	62.29±26.47	303.43±80.51
		AT	36.00±26.48[1)2)]	30.29±27.17[1)2)]	44.00±24.64[1)]	38.29±29.25[1)2)]	45.14±25.82[1)]	193.71±52.42[1)2)]
Control	35	BT	65.71±29.73	57.71±26.91	73.14±22.72	60.00±29.10	61.71±30.82	318.29±62.38
		AT	48.57±25.80[1)]	46.29±18.64	50.29±23.45[1)]	50.86±22.93	49.14±23.93	245.14±47.36[1)]

Note: BT=Before treatment; AT=After treatment; compared with the same group before treatment, 1) P<0.05; compared with the control group after treatment, 2) P<0.05

3.3.3 Comparison of the SDS score

There was no significant difference in SDS score between the two groups before treatment (P>0.05). After treatment, the intra-group difference in SDS score of the control group was not statistically significant (P>0.05), while SDS score of the observation group was significantly lower than that before treatment (P<0.05). The SDS score of the observation group was lower than that of the control group after treatment, and the difference was statistically significant (P<0.05), (Table 4).

Table 4. Comparison of the SDS score between the two groups ($\bar{x}$ ±s, point)

Group	*n*	Before treatment	After treatment
Observation	35	71.03±13.68	51.17±12.92[1)2)]
Control	35	66.54±10.85	60.69±16.26

Note: Compared with the same group before treatment, 1) $P<0.05$; compared with the control group after treatment, 2) $P<0.05$

3.4 Observation on adverse reactions

One patient in the observation group had fainted during the first acupuncture treatment. There were 5 minor adverse reaction cases in the control group: 2 cases of rash, 1 case of pruritus and 2 cases of nausea. There were no severe adverse reactions in the two groups.

4 Discussion

The pathogenesis of IBS is complex. Currently, it is considered to be related to abnormal intestinal motility, visceral hypersensitivity, inflammatory response and intestinal dysbacteriosis[15]. Besides gastrointestinal symptoms such as abdominal pain, diarrhea and abdominal distension, accompanied depressive symptom is also a main clinical feature. IBS and depressive symptom interact as both cause and effect. The two easily formed into a vicious cycle if the course of disease is prolonged, resulting in an aggravation of clinical symptoms. The brain-intestinal axis theory discovered in recent years explains this phenomenon quite well[16]. The brain-intestinal axis is the bridge between brain and gastrointestinal tract. If either side of the brain or intestine has a problem, it is very much likely to involve the other side[17]. For example, depression can affect gastrointestinal function through autonomic nervous system and neuroendocrine regulation; IBS can induce and aggravate depression through immune, neurological, endocrine and intestinal bacterial flora pathway[18-19].

IBS-D has no direct corresponding disease name in Chinese medicine. It belongs to diarrhea, abdominal pain and abdominal distension in TCM. Generally, IBS-D is considered to be caused by dysfunction of liver and spleen. The liver qi stagnation causes abnormal qi movement, resulting in the damage of spleen qi, and inducing abdominal pain and diarrhea. Stagnation of liver qi and spleen deficiency is the basic pathogenesis of this disease.

Coordinating liver and spleen is the key for acupuncture to treat the depressive symptom of IBS-D. Most acupoints are selected from the Stomach Meridian, the Spleen Meridian and the Liver Meridian. The location of IBS-D is large intestine and small intestine, and the location of the depressive symptom is brain. The lower He-Sea point of small intestine and the Front-Mu point of large intestine are all the acupoints of the Stomach Meridian. The running course of the Stomach Meridian is related to gastrointestinal tract and brain. In clinic, points for regulating liver and spleen mostly are Taichong (LR 3), Zusanli (ST 36), Shangjuxu (ST 37), Sanyinjiao (SP 6), Tianshu (ST 25), Baihui (GV 20) and Yintang (GV 29)[20-21]. The combination of these acupoints can disperse the stagnated liver qi and invigorate the spleen, regulate qi movement to relieve diarrhea, fortify the brain and harmonize the spirit.

In this study, it was suggested that acupuncture method of regulating liver and spleen could improve the scores of the degree of abdominal pain, the frequency of abdominal pain, the degree of abdominal distension, defecation satisfaction and life interference and the total IBS-SSS score, and was generally superior to oral intake of pinaverium bromide tablets, especially for the degree of abdominal pain, the frequency of abdominal pain and defecation satisfaction. This therapy also had an obviously better effect than pinaverium bromide tablets in improving SDS score. The results of this study indicated that acupuncture method of regulating liver and spleen could improve the gastrointestinal symptoms and depressive symptom of patients with IBS-D at the same time and had high safety.

However, there were some limitations in this trial such as a small sample size, short intervention and observation and no mechanism research involved. Therefore, for further research, it requires multi-centered clinical trial with a large sample size, high quality, long-term observation of efficacy and follow-up, and deep exploration of the possible mechanism of acupuncture, so as to provide more accurate and reliable clinical and theoretical basis for the effect of acupuncture in treating the depressive symptom in IBS-D.

Conflict of Interest

The author 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.

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