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Special Topic for 973 Program

Effect of electroacupuncture and herbal cake-partitioned moxibustion on anxiety and depression in patients with Crohn's disease in remission

电针和隔药灸对缓解期克罗恩病患者焦虑和抑郁情绪的影响

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Abstract

Objective: To observe the effect of electroacupuncture (EA) and herbal cake-partitioned moxibustion on anxiety and depression in patients with Crohn's disease (CD) in remission.

Methods: Sixty CD cases were randomly allocated into an EA group (n=30) and an herbal cake-partitioned moxibustion group (n=30) using the random number table by the ratio of 1:1. In addition, 30 healthy subjects were included in a control group. Bilateral Tianshu (ST 25), Qihai (CV 6) and Zhongwan (CV 12) were used in the EA and herbal cake-partitioned moxibustion groups. The treatment was done 3 times a week, for a total of 12 weeks. The efficacy was evaluated using self-rating anxiety scale (SAS), self-rating depression scale (SDS) and traditional Chinese medicine (TCM) symptom scores.

Results: Before treatment, the SAS and SDS scores in CD patients were remarkably higher than those in healthy subjects. After EA or herbal cake-partitioned moxibustion treatment, the SAS and SDS scores were significantly decreased in both groups, showing significant intra-group differences (P<0.05); the symptom scores of abdominal pain (severity, frequency and duration), bowel sounds/flatus and general fatigue were significantly decreased, showing significant intra-group differences (P<0.05); however, there were no between-group statistical differences (P>0.05).

Conclusion: Both EA and herbal cake-partitioned moxibustion can significantly decrease abnormally high SAS and SDS scores in CD patients as well as TCM symptom scores. The two therapies share similar effects in alleviating common symptoms and improving anxiety and depression.

Keywords: Acupuncture Therapy; Electroacupuncture; Moxibustion Therapy; Indirect Moxiubustion; Acupuncture-moxibustion Therapy; Crohn Disease; Depression; Anxiety

【摘要】目的：观察电针和隔药灸对缓解期克罗恩病(Crohn's disease, CD)患者焦虑和抑郁情绪的影响。**方法：**将60例符合纳入标准的患者按照1:1比例按随机数字表随机分为电针组和隔药灸组，纳入30例健康受试者作对照。电针组或隔药灸组均选取双侧天枢，气海和中脘，电针组患者采用电针治疗，隔药灸组患者采用隔药灸治疗，每星期治疗3次，共治疗12星期。以自评焦虑量表(self-rating anxiety scale, SAS)、自评抑郁量表(self-rating depression scale, SDS)及中医症状积分为观察指标进行疗效评价。**结果：**与健康受试者相比，CD患者SAS和SDS评分显著增加。电针和隔药灸治疗后，两组患者SAS和SDS评分均显著降低，与本组治疗前有统计学差异(P<0.05)；患者腹痛(程度、频次、时间)及肠鸣矢气、神疲乏力症状积分显著降低，与本组治疗前有统计学差异(P<0.05)，两种疗法间差异无统计学意义(P>0.05)。**结论：**电针和隔药灸均能降低CD患者异常增高的SAS、SDS评分及常见中医症状积分，在缓解临床常见症状的同时改善其焦虑和抑郁情绪，两种疗法作用相当。

【关键词】针刺疗法；电针；灸法；间接灸；针灸疗法；克罗恩病；抑郁；焦虑

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Crohn's disease (CD) is a chronic, recurrent inflammatory bowel disorder (IBD) that may affect any part of the gastrointestinal tract. Patients often present with persistent diarrhea, abdominal pain, and weight loss. This condition may greatly affect patients' quality of life and place a heavy burden to social and medical resources[1]. Studies have confirmed that psychosocial stress is linked to the pathogenesis of CD[2-4]. It's estimated that 31.3%-40.2% patients in remissive stage experience depression and/or anxiety and up to 80% and 60% CD patients experience either anxiety or depression in active stage[5-8]. Anxiety or depression can severely disturb patients' social and family life.

Our research team has been engaged in the basic and clinical studies on treating CD with acupuncture and moxibustion for years[9-16]. Clinical observation has shown that different treatment protocols should be applied to different CD stages, and electroacupuncture (EA) or herbal cake-partitioned moxibustion can be an option for remissive CD. The purpose of this study is to observe the effect of EA and herbal cake-partitioned moxibustion on anxiety and depression in CD patients and provide scientific evidence for the role of acupuncture and moxibustion in CD management.

1 Clinical Data

1.1 Diagnostic criteria

This was based on the diagnostic criteria of CD from the Consensus on Diagnosis and Treatment Norms for Inflammatory Bowel Disease (2007, Jinan, China), coupled with a combination of clinical, radiological, endoscopic, and histological findings[17].

1.2 Inclusion criteria

Those who met the diagnostic criteria; at least 6 months of remission [Crohn's disease activity index (CDAI)≤150]; aged between 18 and 68 years; did not receive acupuncture and moxibustion treatment in the last 3 months; and having signed the informed consent.

1.3 Exclusion criteria

Pregnant, planned to be pregnant, and breast-feeding women; took corticosteroids, immunosuppressants, biological agents, or psychotropic drugs in the last 3 months; a family history of mental or neurologic conditions; having learning disabilities; neurosurgical or other neurological conditions related to brain injury, cerebrovascular damage, head trauma or loss of consciousness; and having complications of cardiac, hepatic or renal insufficiency, severe tuberculosis, acute purulent or contagious disease and acute trauma.

1.4 Statistical methods

The SPSS 16.0 version software was used for data analysis. Upon normality test, the *t*-test was used for measurement data with a normal distribution and the result was expressed as mean ± standard deviation ($\bar{x} \pm s$); and the nonparametric (Mann-Whitney U) test was used for measurement data with a non-normal distribution and the result was expressed as median (lower quartile, upper quartile) [M (Q_{25}, Q_{75})]. The Chi-square test was used for enumeration data. Two-tailed tests were used for statistical significance testing. $P<0.05$ indicated a statistical significance.

1.5 General materials

CD patients treated in IBD Outpatient, Shanghai Research Institute of Acupuncture and Meridian, Shanghai University of Traditonal Chinese Medicine and Endoscopy Center, Zhongshan Hospital Fudan University between June 2012 and January 2014 were recruited as research subjects. These patients were randomly allocated into an EA group and an herbal cake-partitioned group by the ratio of 1:1, 30 cases in each group. In addition, 30 healthy subjects of similar age and gender were included in a control group. There were no significant between-group differences in age, gender, duration and CDAI ($P>0.05$), 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 ($\bar{x} \pm s$, day)	CDAI ($\bar{x} \pm s$, point)
		Male	Female			
EA	30	24	6	35.57±10.37	5.45±4.26	76.50±42.14
Moxibustion	30	18	12	33.47±12.73	6.00±4.20	78.78±49.27
Statistical value		2.857[1)]		0.700[2)]	−0.503[2)]	−0.108[2)]
P value		0.091		0.486	0.617	0.914

Note: 1) x^2 value; 2) *t* value

2 Treatment Methods

2.1 Herbal cake-partitioned moxibustion group

Points: Bilateral Tianshu (ST 25), Qihai (CV 6) and Zhongwan (CV 12).

Ingredients of the herbal cake: *Fu Zi* (*Radix Aconiti Lateralis Praeparata*), *Huang Lian* (*Rhizoma Coptidis*), *Mu Xiang* (*Radix Aucklandiae*), *Hong Hua* (*Flos Carthami*), *Dan Shen* (*Radix et Rhizoma Salviae Miltiorrhizae*), *Dang Gui* (*Radix Angelicae Sinensis*), etc.

Method: Ground the above ingredients into fine powder, filtered through a 100-mesh sieve and placed into a sealed bag. Then mixed 2.0 g powder and 3 g malt sugar with warm water and compressed the thick paste into herbal cakes of 23 mm in diameter and 5 mm in thickness using a specific mold. Put the herbal cakes on the points and placed ignited moxa stick pieces of 16 mm in length and 1.8 g in weight over the cakes, 2 cones for each point. The treatment was done once every two days, 3 times a week, for a total of 12 weeks (36 times).

2.2 EA group

Points: Same as that in the moxibustion group.

Method: After routine sterilization, the above points were punctured 20-25 mm using filiform needles of 0.30 mm in diameter and 40 mm in length (manufactured by Suzhou Medical Appliance Factory Co., Ltd., China). Upon arrival of qi, the electrodes of the electric stimulator (HANS-100) were connected to the left-sided Tianshu (ST 25) and Qihai (CV 6) (one pair) and right-sided Tianshu (ST 25) and Zhongwan (CV 12) (another pair) respectively, using the sparse-dense wave, a frequency of 2 Hz/100 Hz and electric current of 1-2 mA. The needles were retained for 30 min. The treatment was done once every two days, 3 times a week, for a total of 12 weeks (36 times).

3 Efficacy Observation

3.1 Observation items

3.1.1 Self-rating anxiety scale (SAS)[18] and self-rating depression scale (SDS)[19]

The SAS and SDS were used to evaluate anxiety and depression of CD patients and healthy subjects. Both SAS and SDS consist of 20 items rated on a 1-4 Likert type scale. The final score is derived by the total SAS score timing the weight factor 1.25. According to the criteria in China, SAS＞50 points indicates anxiety. Specifically, 50-59 points: mild anxiety; 60-69 points: moderate anxiety; and ＞60 points: severe anxiety. SDS ＞53 points indicates depression. Specifically, 53-62 points: mild depression; 63-72 points: moderate depression; and ＞72 points: severe depression[20].

3.1.2 TCM symptom scores

In Chinese medicine, CD falls under the category of 'diarrhea', 'abdominal pain' or 'intestinal abscesses'. Based on the symptom grading criteria for 'diarrhea' in the *Guiding Principles for Clinical Study of New Chinese Medicines*[21], this study mainly observed abdominal pain (severity, frequency and duration), bowel sounds/ flatus and general fatigue. These symptoms had 4 grades. Grade 0: absence of symptoms; grade 1: mild symptoms; grade 2: moderate symptoms; and grade 3: severe symptoms.

3.2 Anxiety and depression comparison between CD patients and healthy subjects

It has shown that 23.3% CD patients experienced anxiety or depression and 15% of them had mild/ moderate anxiety and 18.3% had mild/moderate depression. The SAS and SDS scores in CD patients were significantly higher than that in healthy subjects and there were significant between-group difference (P＜0.05), (Table 2).

Table 2. Comparison of anxiety and depression between CD patients and healthy subjects ($\bar{x}$ ±s, point)

Group	n	SAS	SDS
CD	60	39.29±9.13	45.46±10.45
Healthy control	30	29.96±3.76	35.50±6.38
t value		5.363	4.673
P value		0.000	0.000

3.3 Effect of herbal cake-partitioned moxibustion and EA on anxiety and depression in CD patients

3.3.1 Effect of herbal cake-partitioned moxibustion and EA on anxiety in CD patients

There were no statistical differences in baseline data between the moxibustion group and EA group (P ＞ 0.05), indicating that the two groups were comparable. After treatment, there were significant intra-group differences in SAS scores (P ＜ 0.01); however, there was no significant between-group difference (P＞0.05), indicating that both methods can significantly decrease SAS scores and improve anxiety with a similar effect (Table 3).

Table 3. Comparison of SAS scores before and after treatment [M (Q_{25}, Q_{75}), point]

Group	n	Before treatment	After treatment	Difference before and after treatment	Z value	P value
EA	30	39.38 (32.50,46.25)	35.63 (30.94, 40.31)[1)]	6.25 (−1.25, 11.25)	−0.474	0.635
Moxibustion	30	36.88 (31.25,43.13)	32.50 (28.75, 39.06)[1)]	3.75 (0.00, 7.50)		

Note: The intra-group comparison before and after treatment, 1) P＜0.01; Z value and P value are between-group differences before and after treatment

3.3.2 Effect of herbal cake-partitioned moxibustion and EA on depression in CD patients

There were no statistical differences in baseline data between the moxibustion group and EA group ($P > 0.05$), indicating that the two groups were comparable. After treatment, there were significant intra-group differences in SDS scores ($P < 0.01$); however, there was no significant between-group difference ($P>0.05$), indicating that both methods can significantly decrease SDS scores and improve depression with a similar effect (Table 4).

3.4 Effect of herbal cake-partitioned moxibustion and EA on common symptoms in CD patients

3.4.1 Effect of herbal cake-partitioned moxibustion and EA on abdominal pain (severity, frequency and duration)

Before treatment, there was no statistical difference in baseline abdominal pain score (severity, frequency and duration) between the moxibustion group and EA group ($P>0.05$), indicating that the two groups were comparable. After treatment, there were significant intra-group differences in abdominal pain severity, frequency and duration in the EA group ($P<0.01$, $P < 0.01$, $P < 0.05$) and herbal cake-partitioned moxibustion group (all $P<0.01$); however, there were no significant between-group differences in abdominal pain severity, frequency and duration (all $P>0.05$), indicating that both methods can significantly alleviate abdominal pain severity, frequency and duration with a similar effect (Table 5).

3.4.2 Effect of herbal cake-partitioned moxibustion and EA on bowel sounds/flatus

Before treatment, there was no statistical difference in baseline bowel sounds/flatus score between the moxibustion group and EA group ($P>0.05$), indicating that the two groups were comparable. After treatment, there were significant intra-group differences in bowel sounds/flatus ($P<0.01$); and there were no significant between-group differences in bowel sounds/flatus ($P > 0.05$), indicating that both methods can significantly alleviate bowel sounds/flatus with a similar effect (Table 6).

3.4.3 Effect of herbal cake-partitioned moxibustion and EA on general fatigue

Before treatment, there was no statistical differencee in baseline general fatigue score between the moxibustion group and EA group ($P>0.05$), indicating that the two groups were comparable. After treatment, there were significant intra-group differences in general fatigue ($P<0.01$, $P<0.05$); and there was no significant between-group difference in general fatigue ($P>0.05$), indicating that both methods can significantly alleviate bowel sounds/flatus with a similar effect (Table 7).

Table 4. Comparison of SDS scores before and after treatment [M (Q_{25}, Q_{75}), point]

Group	*n*	Before treatment	After treatment	Differences before and after treatment	*Z* value	*P* value
EA	30	47.50 (38.75, 53.75)	40.00 (35.94, 47.81)[1)]	6.88 (1.25, 11.25)	−0.081	0.935
Moxibustion	30	42.50 (36.25, 51.25)	36.25 (29.69, 4 2.50)[1)]	5.63 (−0.31, 10.63)		

Note: The intra-group comparison before and after treatment, 1) $P<0.01$; *Z* value and *P* value are between-group differences before and after treatment

Table 5. Comparison of abdominal pain scores before and after treatment [M (Q_{25}, Q_{75}), point]

Abdominal pain	EA group (*n*=30)			Herbal cake-partitioned moxibustion group (*n*=30)		
	Before treatment	After treatment	D-value	Before treatment	After treatment	D-value
Severity	1.0 (0.0, 1.0)	0.0 (0.0, 1.0)[1)]	0.0 (−1.0, 0.0)	1.0 (0.0, 1.0)	0.0 (0.0, 1.0)[1)]	0.0 (−1.0, 0.0)
Frequency	1.5 (0.0, 3.0)	0.0 (0.0, 2.0)[1)]	0.0 (−1.3, 0.0)	2.0 (0.0, 3.0)	0.0 (0.0, 1.0)[1)]	−1.0 (−2.0, 0.0)
Duration	1.0 (0.0, 1.0)	0.0 (0.0, 1.0)[2)]	0.0 (−0.3, 0.0)	1.0 (0.0, 2.0)	0.0 (0.0, 1.0)[1)]	0.0 (−1.0, 0.0)

Note: D-value=Differences before and after treatment; the intra-group comparison before and after treatment, 1) $P<0.01$, 2) $P<0.05$

Table 6. Comparison of bowel sounds/flatus scores before and after treatment [M (Q_{25}, Q_{75}), point]

Group	*n*	Before treatment	After treatment	Differences between and after treatment	*Z* value	*P* value
EA	30	1.0 (0.0, 2.0)	1.0 (0.0, 1.0)[1)]	0. 0 (−1.0, 0.0)	−0.139	0.889
Moxibustion	30	1.0 (0.0, 1.0)	0.0 (0.0, 1.0)[1)]	0.0 (−1.0, 0.0)		

Note: The intra-group comparison before and after treatment, 1) $P<0.01$; *Z* value and *P* value are between-group differences before and after treatment

Table 7. Comparison of general fatigue scores before and after treatment [M (Q_{25}, Q_{75}), point]

Group	*n*	Before treatment	After treatment	Differences before and after treatment	*Z* value	*P* value
EA	30	1.0 (0.8, 2.0)	0.5 (0.0, 1.0)[1)]	−0.5 (−1.0, 0.0)	−0.950	0.342
Moxibustion	30	1.0 (0.0, 1.0)	0.5 (0.0, 1.0)[2)]	0.0 (−1.0, 0.0)		

Note: The intra-group comparison before and after treatment, 1) $P<0.01$; 2) $P<0.05$; *Z* value and *P* value are between-group differences before and after treatment

4 Discussion

Psychosocial stress (anxiety and depression) has been confirmed to be closely linked to the pathogenesis of CD[2-4]. Although in remission, CD patients in this study showed significantly higher SAS and SDS scores than healthy subjects and up to 23.3% patients experienced mild to moderate anxiety or depression. This indicates that anxiety or depression may be potentially associated with disease progression. As a result, active intervention and control of anxiety or depression are of great significance to alleviate CD symptoms and improve patients' quality of life.

In Chinese medicine, deficiency of the spleen and stomach may cause dampness to obstruct the flow of qi. Over time, yang deficiency of the spleen and kidney and internal stagnation of dampness and stasis may contribute to CD symptoms[22-25]. In this study, bilateral Tianshu (ST 25), Qihai (CV 6) and Zhongwan (CV 12) were used for EA and herbal cake-partitioned moxibustion, because they regulate qi and blood, alleviate pain, supplement qi, harmonize the stomach and stop diarrhea. The findings of this study have shown that both EA and herbal cake-partitioned moxibustion can significantly decrease SAS and SDS scores and improve patients' anxiety and depression. Moreover, the two methods share similar effects in alleviating abdominal pain (severity, frequency and duration), bowel sounds/flatus and general fatigue. Previous studies have also suggested that acupuncture and moxibustion can significantly decrease CDAI scores, improve patients' quality of life and alleviate inflammatory symptoms[9]. This study has proven that acupuncture and moxibustion can not only alleviate clinical symptoms and inflammation but also improve anxiety and depression. This study selected points of the Stomach Meridian and Conception Vessel instead of points that nourish heart mind and soothe liver qi. Consequently, the effect of EA or herbal cake-partitioned moxibustion on anxiety and depression might be based on alleviation of clinical symptoms. Similar effects of the two treatment protocols indicate that either protocol is effective for remissive CD patients. However, for patients who are scared of needles, herbal cake-partitioned moxibustion is more convenient and can be done at home.

As for the limitation of this study, it's better to have another control group that uses points for nourishing heart mind and soothing liver qi, such as Shenmen (HT 7) and Taichong (LR 3). This can allow us to observe and compare the effect of two treatment protocols (using different groups of points) and provide more scientific evidence for acupuncture treatment of CD.

In summary, the anxiety and depression in remissive CD patients are significantly more severe than those in healthy subjects. EA and herbal cake-partitioned moxibustion have similar effects in alleviating clinical symptoms and improving anxiety and depression. Clinically, patients can choose either method. However, herbal cake-partitioned moxibustion is more convenient and much easier to be accepted by CD patients. Therefore, it has greater potential in clinical application.

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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