DOI: 10.1007/s11726-016-0931-5

Special Topic for 973 Program

Observation on the effects of different partitioned moxibustion in treating ulcerative colitis

不同隔物灸治疗溃疡性结肠炎临床观察

Yang Ling (杨玲)¹, Zhao Ji-meng (赵继梦)¹, Guan Xin (关鑫)², Wang Xiao-mei (王晓梅)¹, Zhao Chen (赵琛)³, Liu Hui-rong (刘慧荣)¹, Wu Lu-yi (吴璐一)⁴, Ji Jun (纪军)¹, Cheng Fang (程芳)⁵, Liu Xi-ru (刘希茹)², Wu Huan-gan (吴焕淦)¹

- 1 Shanghai Research Institute of Acupuncture and Meridian, Shanghai 200030, China
- 2 Shuguang Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai 200021, China
- 3 Yueyang Hospital of Integrated Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai 200437, China
- 4 Shanghai Qigong Research Institute, Shanghai 200030, China
- 5 Jinyang Community Health Service Center, Pudong New Area, Shanghai, Shanghai 200136, China

Abstract

Objective: To observe the clinical effect and syndrome scores improvements of herbal cake-partitioned moxibustion (HPM) and ginger-partitioned moxibustion (GPM) in treating ulcerative colitis (UC).

Methods: A total of 65 eligible cases were randomly divided into a HPM group (n=32) and a GPM group (n=33) according to their visiting order. Bilateral Tianshu (ST 25) and Dachangshu (BL 25) were selected for the HPM or the GPM treatment once daily, 12 d as a treatment course with a 3-day interval, 6 courses in all. The clinical effect, syndrome scale and Mayo scale were evaluated and compared between the two groups.

Results: Of the 65 cases enrolled, 2 cases dropped out in the HPM group and 3 cases dropped out in the GPM group, 30 cases of each group finished the treatment courses. The total effective rate is 93.3% in HPM group and 86.7% in the GPM group, there was no statistically significant difference in the total effective rate between the two groups (P > 0.05); there were statistically significant differences between the two groups in score evaluation of lasting time of abdominal pain and frequency of diarrhea, HPM is prior to GPM (P = 0.032, P = 0.044). There are no statistical significant differences between the two groups in scores evaluation of general symptom, three main symptoms, quality of life (QOL), frequency and severity of abdominal pain, times, and pattern of diarrhea (all P > 0.05). There was a statistical significant difference in the improvement of Mayo score between the two groups, and HPM was superior to GPM (P = 0.048).

Conclusion: HPM and GPM are both promising ways to treat UC, and the total effect is quite similar. HPM is superior to GPM in the improvement of lasting time of abdominal pain and frequency of diarrhea, and also the Mayo score.

Keywords: Moxibustion Therapy; Indirect Moxibustion; Colitis, Ulcerative; Diarrhea; Point, Tianshu (ST 25); Point, Dachangshu (BL 25)

【摘要】目的:观察隔药饼灸和隔萎灸治疗溃疡性结肠炎(ulcerative colitis, UC)的临床疗效和症状评分改善情况。方法:将 65 例慢性 UC 患者随机分为隔药饼灸组(n=32)和隔萎灸组(n=33)。两组取相同穴位,即双侧天枢和大肠俞,分别采用隔药饼灸和隔萎灸治疗,每天治疗 1 次, 12 次为 1 疗程,疗程间休息 3 d,共治疗 6 个疗程。观察并比较两组临床疗效、症状评分以及 Mayo 评分改善状况。结果:治疗过程中,隔药饼灸组脱落 2 例,隔姜灸组脱落 3 例,最终每组 30 例纳入统计。治疗后,隔药饼灸组总有效率为 93.3%,隔姜灸组总有效率为 86.7%,两组间差异无统计学意义(P>0.05)。隔药饼灸组腹痛时间和腹泻频度改善情况均优于隔姜灸组(P=0.032, P=0.044)。治疗后,总体症状评分,主要症状评分,生活质量改善,腹痛频度、程度评分以及腹泻次数、性状评分比较,组间差异均无统计学意义(均 P>0.05)。隔药饼灸组患者 Mayo 评分改善情况优于隔姜灸组(P=0.048)。结论:隔药饼灸和隔姜灸均是治疗慢性 UC 的有效方法,两者总体疗效相当;隔药饼灸在改善腹痛时间评分、腹泻频度评分和 Mayo 评分方面优于隔姜灸组。

Author: Yang ling, M.D., postdoctor Joint Corresponding Author: Wu Huan-gan, professor, researcher, doctoral supervisor. E-mail: wuhuangan@126.com; Liu Hui-rong, researcher, doctoral supervisor. E-mail: lhr_tcm@139.com



【关键词】灸法;间接灸;结肠炎,溃疡性;腹痛;腹泻;穴,天枢;穴,大肠俞 【中图分类号】R245.8 【文献标志码】A

Ulcerative Colitis (UC) is a refractory bowel disease mainly involving the colon mucosa with chronic inflammatory and recurrent ulcer. The main symptoms are continuous or repetitive diarrhea mixed with blood and mucus, abdominal pain, tenesmus and varying systemic symptoms. Diffuse inflammation and the generalized hyperemia of the shallow mucous membrane more likely occur in early stage, then mucosal edema, erosion and ulcer. In the process of its repeated attacks, the formation of intestinal fibrosis and narrowing were followed^[1]. Reported cases of UC increased year by year in China, and the incidence of which topped the list in Asian countries^[2]. UC is closely associated with colon cancer, about 0.64% of UC will develop into colorectal cancer, and the longer the duration, the higher the risk of colorectal cancer^[3].

Etiology and pathogenesis of UC are complicated and not fully understood yet. Generally, it's believed that the pathology is mainly associated with immunologic, infectious and genetic factors. UC has been listed as one of the refractory diseases by World Health Organization (WHO) for the long duration and high recurrence rate^[4]. Western medicine mainly uses drugs, nutritional support, psychotherapy and surgery, which has a number of side-effects and heavy economic burden, while Chinese medicine has the extraordinary advantage of assured curative effect. A large number of clinical and experimental researches certified the effectiveness of moxibustion in treating UC[5-7], on the basis of which we try to observe the effect of herbalpartitioned moxibustion (HPM) and ginger-partitioned moxibustion (GPM) to treat UC in remission, and to further compare the effect of herb and ginger in the moxibustion to support the clinical data.

1 Clinical Data

1.1 Diagnostic criteria of Western medicine

UC patients were selected according to the revised Diagnostic Criteria of Inflammatory Bowel Disease (Jinan) in 2007 national conference^[8].

Clinical manifestation: Continuous or repeated diarrhea, mucus purulent blood stools with abdominal pain, tenesmus and varying systemic symptoms.

Colonoscopy: Lesions always start from the rectum, and distribute with continuity and diffusion. Texture fuzzy, disorder, congestion, edema, brittle, bleeding and purulent secretion were found on the mucosal blood vessels, and also membrane coarse or fine grained appearance changes could be seen. Diffuse multiple erosions or ulcers appeared in severe lesions; in the remission stage, colonic pouch became shallow, dull or

disappeared, as well as pseudopolyps and bridge-like mucous membrane, etc.

X-ray Barium enema examination: Mucous membrane coarse and (or) grain appearance change; jigsaw or burr sample change could be seen on the intestinal canal edge, and multiple small filling defect could be found on the intestinal wall; the bowel tract became shorter, and the bag sac disappeared into a 'lead-pipe'.

Mucosal biopsy: Bacterial dysentery, amebic dysentery, chronic schistosomiasis, intestinal tuberculosis and other infectious colitis and Crohn's desease (CD), ischemic colitis, and radioactive colonitis were excluded.

In conclusion, typical clinical manifestations, and at least one of the three typical changes in endoscopic and (or) mucosa biopsy can diagnose the disease; typical clinical manifestations, and at least one of the three typical changes in X-ray Barium enema can diagnose the disease; typical changes in endoscopic and X-ray barium enema, without typical clinical manifestations, can be diagnosed as the suspected case, and need to observe the clinical manifestation as well.

1.2 Syndrome differentiation standards of traditional Chinese medicine (TCM)

UC can be divided into three types, spleen deficiency with dampness, liver stagnation with spleen deficiency and yang deficiency of the spleen and kidney according to the Consensus of TCM Diagnosis and Treatment of Ulcerative Colitis at the 21st Academic Conference of Spleen and Stomach Disease Branch, China Association of TCM in 2010^[9].

1.2.1 Spleen deficiency with dampness

Primary symptoms: ① Loose stools, mucus with white more than red, or white frozen; ② a light red tongue with teeth marks, white greasy coating.

Secondary symptoms: ① Abdominal distending pain; ② abdominal fullness and distention; poor appetite; ③ lassitude and mental fatigue with reluctance to talk; ④ thready weak pulse or thready slippery pulse.

1.2.2 Liver stagnation with spleen deficiency

Primary symptoms: ① Diarrhea complicated with abdominal pain, and the pain alleviates after diarrhea; ② stools frequency always increased by emotion or dietary factors.

Secondary symptoms: ① Loose stools or mucoid stools; ② depression or anxiety; ③ belching, poor appetite with abdominal distension; ④ a light red tongue with thin white coating; ⑤ wiry or wiry thready pulse.

1.2.3 Yang deficiency of the spleen and kidney

Primary symptoms: ① Chronic diarrhea with white frozen even diarrhea with undigested food, or fecal incontinence; ② aversion to cold with cold extremities.

Secondary symptoms: ① Abdominal pain alleviated by warmth and pressure; ② abdominal fullness and poor appetite; ③ lumbar soreness with knee weakness; ④ a pale and swollen tongue, some with teeth marks, thin white and moist coating; ⑤ deep and thready pulse.

For the determination of the three types: 2 primary symptoms (① is necessary) and 2 secondary symptoms should be met; or item ① of the primary symptoms and 3 secondary symptoms should be met.

1.3 Inclusion criteria

Conforming to the diagnostic criteria of UC; with chronic continuous and chronic recurrent type; aged from 18-65 years old; accorded with the syndrome differentiation standards of TCM; willing to join the study and having signed the informed consent.

1.4 Exclusion criteria

UC patients with other types; acute cases or initial onset cases; those who took some medicine (such as glucocorticoids, etc.) that may affect the efficacy evaluation; those who suffering from the infective colitis, ischemic colitis or radioactive colitis; having dysfunction of heart, brain, liver, kidney, or hematopoietic system, or mental disorder; unable to finish the treatment courses.

1.5 Severity evaluation standard

Symptom severity evaluation with reference to the proposed standards in the *Criteria of Diagnosis and Therapeutic Effects of Diseases and Syndromes in Traditional Chinese Medicine*^[10] (four grades according to the severity of the symptoms): 0 point (none), 1 point (mild), 2 points (moderate), 3 points (severe). Patients filled in the syndrome form before treatment. We observed the base line of the main symptoms such as frequency, degree and time of abdominal pain, the times, pattern and frequency of diarrhea and the mucus

purulent blood stools.

1.6 Statistical methods

1.6.1 Random method

The SPSS 15.0 version software was used to generate random numbers, and a sealed envelope method was used to randomly assign subjects to two groups according to their visit orders.

1.6.2 Data processing methods

Analyses were performed using the SPSS 15.0 version software. Mean \pm standard deviation (\overline{x} $\pm s$) was used to describe measurement data with normal distribution. Data with non-normal distribution were described by median (min, max). Two-sample t-test was applied to between-group comparison, and paired-samples t-test was used for inter-group comparison before and after treatment for variables with normal distribution and constant variances. Wilcoxon rank sum test was applied to between-group comparison for the measurement data with non-normal distribution. Enumeration data were analyzed by Chi-square test or signed rank sum test of ranked data. Overall significance was set at 0.05. P < 0.05 was considered as a statistical significance.

1.7 General data

A total of 65 eligible UC patients from the UC Specialist Clinic of Shanghai Research Institute of Acupuncture and Meridian and Endoscopy Center of Zhongshan Hospital were randomly divided into a HPM group (32 cases) and a GPM group (33 cases) according to the random numbers from SPSS 15.0 and their visit orders. Of the 5 dropped-out patients, 2 cases were in the HPM group (1 case went on a business trip, 1 subject got pregnant); versus 3 patients were in the GPM group (1 case went on a business trip, 1 case for a travel and 1 case with no explanation).

At last, data of 60 cases (30 cases in each group) were analyzed. The gender, average age, treatment courses and severity of disease showed no significant differences between the two groups (P > 0.05), indicating that the two groups were comparable (Table 1).

Table 1. Between-group comparison of the base line

Сиохи		Gender (case)		Average age	Mean duration	Average weight	Severity (case)	
Group	n	Male	Female	[median (min, max), year]	[median (min, max), month]	[median (min, max), kg]	Mild	Moderate
HPM	30	13	17	57.0 (26, 65)	24.0 (5, 240)	57.5 (42, 80)	15	15
GPM	30	14	16	53.0 (18, 65)	60.0 (3, 240)	55.5 (40, 80)	21	9
Statistical value		0	$.000^{1)}$	$-1.302^{2)}$	$-0.948^{2)}$	0.111 ³⁾		1.736 ¹⁾
P value		1.000		0.193	0.343	0.912	0.188	

Note: 1) x^2 value; 2) Z value; 3) t value

2 Treatment Methods

2.1 Basic treatments

Patients who were taking Western medicine should quit the medication for one week before joining in the group. Other medications and treatments should also stop during the treatment period. The patients were told to live regular life, keep in a good mood, and avoid eating spicy or greasy food. Eligible patients accepted the basic treatment as take orally taking the Mesalazin Enteric-coated tablets (Huidi, approved by: H19980148, Sunflower Pharmaceutical Group Kamusze Luling Pharmaceutical Co., Ltd., China), 0.5 g each time, 3 times a day.

2.2 HPM

Points: Tianshu (ST 25) and Dachangshu (BL 25).

Methods of making herb pad: Herbs were supplied by Fengxian Dehua Pharmaceutical Factory. Fu Zi (Radix Aconiti, from Sichuan Province), Rou Gui (Cortex Cinnamomi, from Guangxi Zhuang Autonomous Region), Mu Xiang (Radix Aucklandiae, from Yunnan Province), etc. were ground into fine powder and sifted through 100 mesh and stored 250 g/package for use. 2.5 g herbal powder was mixed with 3 g rice wine, then made into pads of 1.9 cm in diameter and 0.5 cm in thickness by mould.

Treatment methods: Patients were asked to lie down on the stomach to expose Dachangshu (BL 25). The herbal pad was placed on the points with 1.5 g moxa cone on the pad (the moxa used was stored for three years, Huatuo Brand, produced by Suzhou East Moxa Factory, China). The moxa cone was made by a mould of 1.8 cm in diameter and 1.5 cm in height. One cone was used for each point. Then the patiens were asked to lie down on the back, and moxibustion was performed at Tianshu (ST 25) with the same method. The treatment was given once daily, 12 times as a treatment course with a 3-day interval, 6 courses in total (Figure 1 and Figure 2).



Figure 1. HPM at Dachangshu (BL 25)



Figure 2. HPM at Tianshu (ST 25)

2.3 **GPM**

Points: Points were selected same as those in the HPM group.

Operation: Fresh ginger was cut along fiber longitudinally into a slice of 0.5 cm in thickness and 1.9 cm in diameter. The ginger was placed on the same points and with same treatment courses as that in the HPM group, one cone was used for each point (Figure 3 and Figure 4).



Figure 3. GPM at Dachangshu (BL 25)



Figure 4. GPM at Tianshu (ST 25)

3 Results

3.1 Observational items

3.1.1 Symptom evaluation

Symptom evaluation with reference to the proposed standards in *Criteria of Diagnosis and Therapeutic Effects of Diseases and Syndromes in Traditional Chinese Medicine*^[10]. Patients filled in the syndrome form after treatment. We observed the improvement of the main symptoms such as frequency, severity and time of abdominal pain, the times, pattern and frequency of diarrhea and the mucus purulent blood stools. Total score of abdominal pain was composed by the score of frequency, severity and times of pain. Total score of diarrhea was composed by the score of times, character and frequency. Score of bloody purulent stools constituted of score of mucus and score of bloody purulent stools. The severity of the disease was in a direct proportion to the score.

3.1.2 Evaluation of disease severity and activity

Disease severity and activity were evaluated by the

improved Mayo activity index^[11]: the sum of total score <2 points, the syndromes relieved; 3-5 points meant mild activity; 6-10 points meant moderate activities; 11-12 points meant severe activity (Table 2).

3.1.3 Evaluation on improvement of quality of life (QOL)

The QOL was assessed by the inflammatory bowel diseases questionnaire (IBDQ) $^{[12]}$, which was used to investigate the feelings of the patient in last 2 weeks, and to evaluate the syndrome, overall feeling and emotion. In the total of 32 questions, the answer of each question has 7 levels: level 1 represents the most severe, for 1 point; level 7 on behalf of the lightest, for 7 points. The sum of the total score was then compared.

3.1.4 Influence of different partitioned moxibustion on colonic mucosa morphology of UC patients

Colonic pathological changes were observed under an optical microscope after hematoxylin-eosin (HE) staining.

Table 2. Improved Mayo activity index

Syndrome	0 score	1 score	2 scores	3 scores
Diarrhea	None	1-2 times/day	3-4 times/day	More than 5 times a day
Hemafecia	None	A litter bit	Obviously	Much blood
Mucous membrane	Normal	Mild brittle	Moderate brittle	Serious brittle with effusion
Doctor's consideration	Normal	Mild	Moderate	Severe

3.2 Criterion of therapeutic effect

The therapeutic effect was evaluated by the total score of syndromes according to the Consensus of TCM Diagnosis and Treatment of Ulcerative Colitis at the 21st Academic Conference of Spleen and Stomach Disease Branch, China Association of TCM in 2010^[9].

Efficacy index = (Total syndromes score before treatment — Total syndromes score after treatment) \div Total syndromes score before treatment \times 100%.

Cured: Syndromes, symptoms disappeared or almost disappeared, efficacy index ≥95%.

Marked effect: Syndromes, symptoms improved obviously, efficacy index \geqslant 70%, <95%.

Improvement: Syndromes, symptoms improved, efficacy index $\ge 30\%$, < 70%.

Failure: Syndromes, symptoms remained no change, efficacy index <30%.

3.3 Results

Through a series of clinical screening, grouping, treatment and observation, the results were as follows. The clinical procedure was shown in the Figure 5.

3.3.1 Between-group comparison of therapeutic efficacy

There were 10 cases markedly improved, 18 cases improved and 2 cases failed in the HPM group. There were 6 cases markedly improved, 20 cases improved and 4 cases failed in the GPM group. The total effective rate in the HPM group was 93.3%, versus 86.7% in the GPM group, showing no statistically significant difference between the two groups by the Mann-Whitney *U* nonparametric test, which showed that the two groups have similar effects in treatment of UC (Table 3).

3.3.2 Between-group comparison of syndromes scores

Inter-group non-parametric test showed that the total syndromes scores evaluations were significantly changed in the two groups (both P < 0.01), which indicated that both methods markedly improved UC syndromes. Also, there were no significance differences in the total syndrome score before and after treatment in the two groups (both P > 0.05), which indicated that the two groups have similar effects in the treatment of UC (Table 4).

3.3.3 Between-group comparison of main symptoms scores

Non-parametric test showed that the abdominal pain, diarrhea and bloody mucopurulent stools score evaluations were all significantly changed in two groups (both P < 0.01), which indicated that both methods markedly improved the abdominal pain, diarrhea and bloody mucopurulent stools of UC patients. Also, there

were no significant differences in abdominal pain, diarrhea and bloody mucopurulent stools scores before and after treatment between the two groups and among the three main syndromes (all P>0.05), which indicated that the two groups had similar effects in improving the abdominal pain, diarrhea and bloody mucopurulent stools of UC (Table 5).

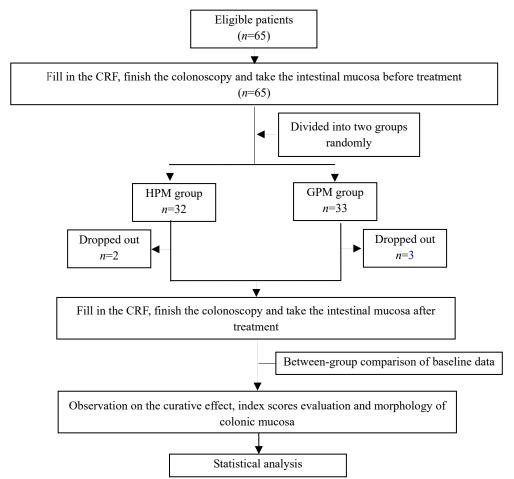


Figure 5. Flow chart of clinical operation

Table 3. Between-group comparison of therapeutic efficacy (case)

Group	n	Marked effect	Improvement	Failure	Z value	P value
HPM	30	10	18	2	1 210	0.197
GPM	30	6	20	4	-1.319	0.187
Total	60	16	38	6		

Table 4. Between-group comparison of syndromes score [M (min, max), point]

Group	n	Before treatment	After treatment	Difference	Z value	P value
HPM	30	18.0 (12, 36)	$7.0(1,20)^{1)}$	10.0 (4, 24)	-4.791	0.001
GPM	30	16.0 (5, 32)	$6.0(2,16)^{1)}$	10.5 (3, 17)	-4.787	0.001
Z		-1.222	-0.022	-1.774		
P		0.222	0.982	0.076		

Table 5. Between-group comparison of main symptoms scores [M (min, max), point]

Main armentama	H	PM group $(n=30)$		GPM group $(n=30)$			
Main symptoms	Before treatment	After treatment	Difference	Before treatment	After treatment	Difference	
Abdominal pain	5.0 (0, 9)	$3.0(0,6)^{1)}$	2.5 (0, 6)	4.0 (0, 9)	$2.0(0,5)^{1)}$	3.0 (0, 6)	
Diarrhea	3.5 (0, 9)	$1.0(0,4)^{1)}$	2.0 (0, 9)	3.0 (0, 8)	$0.5(0,4)^{1)}$	2.0 (0, 5)	
Mucus purulent blood stools	2.0 (0, 6)	$0(0,2)^{1)}$	1.0 (0, 5)	2.0 (0, 5)	$0(0,2)^{1)}$	1.0(0,4)	

Note: Inter-group comparison before and after treatment, 1) P < 0.01

3.3.4 Between-group comparison of the frequency, severity and time of abdominal pain

Non-parametric test showed that the scores of frequency, degree and time of abdominal pain were significantly changed in the two groups (both P < 0.01), indicating that both methods markedly improved the frequency, degree and time of abdominal pain in UC patients. Also, there were no significant differences in frequency and degree of abdominal pain between the two groups (both P > 0.05), while there was a significance difference in shortening the time of abdominal pain between the two groups (P = 0.032), which indicated a better effect in the HPM group than that in the GPM group (Table 6).

3.3.5 Between-group comparison on the times, pattern and frequency of diarrhea

Non-parametric test showed that the scores of times, pattern and frequency of diarrhea were significantly changed in the two groups (both $P \le 0.01$), indicating that both methods markedly improved the times, pattern and frequency of diarrhea in UC patients. Also, there were no significance differences in times and pattern of diarrhea between the two groups, (both

P>0.05), while, there was a significance difference in improving the frequency of diarrhea between the two groups (P=0.044), which indicated a better effect in the HPM group (Table 7).

3.3.6 Between-group comparison of severity and activity of disease

Non-parametric test showed that the Mayo scores were significantly changed in the two groups (both P < 0.01), indicating that both methods markedly improved the Mayo score in UC patients. Also, there was a significant difference in improving the Mayo score evaluation between the two groups (P = 0.048), which indicated a better effect in the HPM group than that in the GPM group (Table 8).

3.3.7 Between-group comparison of IBDQ score

Non-parametric test showed that the IBDQ scores were significantly changed in the two groups (both P < 0.01), indicating that both methods markedly improved the IBDQ score in UC patients. While, there was no significant difference in improving the IBDQ score between the two groups (P > 0.05), which indicated a similar effect in improving the QOL in the two groups (Table 9).

Table 6. Between-group comparison of the frequency, degree and time of abdominal pain [M (min, max), point]

Abdominal pain	HPM group $(n=30)$				GPM group $(n=30)$			
	Before treatment	After treatment	Difference		Before treatment	After treatment	Difference	
Frequency	2.0 (0, 3)	$1.0(0,2)^{1)}$	1.0 (0, 3)		2.0 (0, 3)	$1.0(0,2)^{1)}$	1.0 (0, 3)	
Degree	1.0(0,3)	$0.5(0,2)^{1)}$	1.0 (0, 3)		1.0 (0, 3)	$0.5(0,2)^{1)}$	1.0 (0, 2)	
Time	1.0(0,3)	$0.5(0,2)^{1)}$	$1.0(0,2)^{2)}$		1.0 (0, 3)	$0(0,2)^{1)}$	0 (0, 2)	

Note: Inter-group comparison before and after treatment, 1) P<0.01; compared with the GPM group, 2) P<0.05

Table 7. Between-group comparison of the times,pattern and frequency of diarrhea [M (min, max), point]

Diarrhea	HPM group ($n=30$)				GPM group ($n=30$)			
	Before treatment	After treatment	Difference		Before treatment	After treatment	Difference	
Times	1.0 (0, 3)	$0(0,2)^{1)}$	1.0 (0, 3)		1.0 (0, 3)	$0(0,2)^{1)}$	1.0 (0, 2)	
Character	1.0 (0, 3)	$0(0,1)^{1)}$	1.0 (0, 3)		1.0 (0, 3)	$0(0,2)^{1)}$	1.0 (0, 2)	
Frequency	1.5 (0, 3)	$0(0,2)^{1)}$	$1.0(0,3)^{2)}$		1.0 (0, 3)	$0(0,2)^{1)}$	1.0 (0, 3)	

Note: Inter-group comparison before and after treatment, 1) P < 0.01; compared with the GPM group, 2) P < 0.05

Table 8. Between-group comparison of severity and activity of disease [M (min, max), point]

Group	n	Before treatment	After treatment	Difference	Z value	P value
HPM group	30	4 (0, 8)	2 (0, 4) ¹⁾	$2(0,6)^{2)}$	-4.425	0.001
GPM group	30	3 (2, 5)	$2(0,4)^{1)}$	1 (0, 3)	-4.564	0.001
Z value		-1.548	-0.444	-1.977		
P value		0.122	0.657	0.048		

Note: Inter-group comparison before and after treatment, 1) P < 0.01; compared with the GPM group, 2) P < 0.05

Table 9. Between-group comparison of IBDQ score evaluation [M (min, max), point]

Group	n	Before treatment	After treatment	Difference	Z value	P value
HPM group	30	155.0 (86, 209)	185.5 (130, 222) ¹⁾	-24.5(-79,4)	-4.762	0.001
GPM group	30	161.0 (113, 15)	$189.0 (120, 213)^{1)}$	-21.5(-50,33)	-4.341	0.001
Z value		-0.495	-0.392	-0.843		
P value		0.620	0.695	0.399		

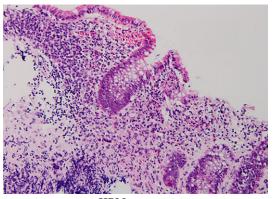
Note: Inter-group comparison before and after treatment, 1) P < 0.01

3.3.8 Morphology of colonic mucosa of UC patients

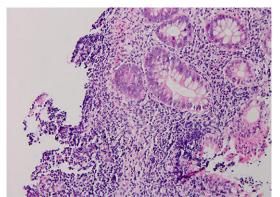
Before treatment, there were missing and damage on the mucosa epithelium, large superficial ulcers, glandular structure damage, and crypt abscesses. Neutrophil aggregation was also found in glands and a large number of inflammatory cells infiltration

surrounded (Figure 6).

After treatment, there were epithelial hyperplasia, neat epithelium and glands on the colonic mucosa, the edema and inflammatory cells infiltration, and a small amount of congestion in organized clearance was also seen in the two groups (Figure 7).

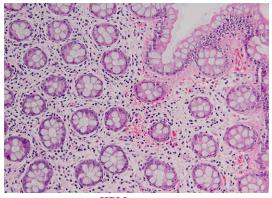


HPM group

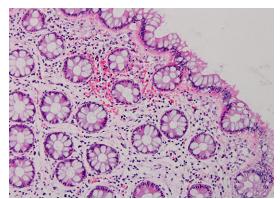


GPM group

Figure 6. Morphology of colonic mucosa before treatment (HE, ×200)



HPM group



GPM group

Figure 7. Morphology of colonic mucosa after treatment (HE, ×200)

4 Discussion

UC is a chronic and recurrent inflammatory intestinal disease, as well as a precancerous disease. It brings great threat to the QOL and life property of people. At present, Western medicine is restricted due to the expensive cost, significant side effects, drug dependence and unstable effects, etc. TCM is showing its unique advantages, especially the moxibustion therapy, in keeping the stable condition and preventing the recurrence of UC. Moxibustion is an effective therapy for prevention and control diseases through the meridian system by igniting moxa to stiulated the points or diseased region. It dredges meridians, warms qi and blood, strengthens the body resistance and eliminates pathogenic factors.

Partitioned moxibustion was first seen in *Zhou Hou Bei Ji Fang* (*Handbook of Prescriptions for Emergencies*) written by Ge Hong (a famous doctor in Jin Dynasty), belonging to indirect moxibustion^[13], performed by placing medicine or other materials between moxa cone and surface of the body. It includes HPM, GPM and garlic-partitioned moxibustion, etc. due to the difference of partition. At present, HPM and GPM therapy have been widely applied in clinic.

HPM is an effective therapy for the intestinal diseases such as UC, CD, which has been confirmed by a long-term study from experiment to clinic. Professor Wu HG applied this therapy based on years of clinical experiences and the further study of 'warming and tonifying spleen-stomach' of Luo Tian-yi (a famous doctor in Yuan Dynasty). It has been confirmed that HPM has reliable effect on UC in the previous study of our group^[5-7,14-15]. For mild and moderate UC patients, HPM can improve the abdominal pain, diarrhea, mucus, bloody purulent stools, and abdominal distension. It can also restrain or eliminate the expressions inflammatory cytokines of colonic mucosa interleukin (IL)-8, intercellular adhesion molecule (ICAM)-1, cyclooxygenase (COX)-2, tumor necrosis factor (TNF)- α and intestinal epithelial cells human leukocyte antigen (HLA)-DR, increase T8⁺ cells count and adjust the disorder of T cell subgroup ratio [14-16], confirming that HPM can regulate the body through multiple levels, multiple links and multi-channels.

This research compared the clinical effects of HPM and GPM for chronic UC from multiple aspects such as the general symptoms, main symptoms, QOL improvement, abdominal pain (frequency, degree and time), diarrhea (times, pattern and frequency), Mayo ratings and pathology. Results showed that HPM and GPM could both obviously improve the total effective

rate, general symptom score, QOL, abdominal pain (frequency, degree and time), diarrhea (times, pattern and frequency). Between-group comparison showed a similar effect in the two groups, which indicated that GPM is also an effective therapy in treating UC. It coincides with the conclusion of a Meta analysis on GPM for UC from Sun TA, $et\ al^{[17]}$.

Partition is one of the key factors for the effect of partitioned moxibustion. Fu Zi (Radix Aconiti) is the sovereign medication; Rou Gui (Cortex Cinnamomi), Dan Shen (Radix Salviae Miltiorrhizae), Hong Hua (Flos Carthami) and Mu Xiang (Radix Aucklandiae) are the assistant. Fu Zi (Radix Aconiti) and Rou Gui (Cortex Cinnamomi) have a function of warming yang, dispelling cold and resolving dampness; Mu Xiang (Radix Aucklandiae) can promote the circulation of gi, regulate the middle Jiao and relieve pain. The three herbs used together have the function of warming yang and tonifying the spleen, smoothing qi and regulating the middle jiao, so that to treat the disease from the root. Huang Lian (Rhizoma Coptidis), Dan Shen (Radix Salviae Miltiorrhizae), and Hong Hua (Flos Carthami) used together have the function of clearing heat and removing dampness, smoothing gi and dispersing blood stasis. GPM is an important part of indirect moxibustion. Ginger possesses a pungent property. It's slight warm, and goes into the Lung Meridian, Spleen Meridian and Stomach Meridian, releasing the exterior and expelling cold, and warming middle Jiao to stop vomiting. Gingerol is a unique component of ginger, and it can stimulate gastrointestinal mucosa to strengthen the blood circulation and digestion, regulate the intestine by warming the middle Jiao and dispelling cold, and invigorate the spleen to arrest diarrhea. GPM is always used to treat the deficiency-cold in spleen and stomach. The UC patients selected in this study possessed three TCM syndromes, and they had a same pathogenesis which was deficiency-cold in spleen. That's why the two partitioned moxibustion both had good therapeutic effect. The further analysis of the results showed that HPM was superior to GPM in shortening the time of abdominal pain, and improving the frequency of diarrhea and Mayo score. Professor Wu HG, et al consider that the deficiency of spleen and stomach can be always seen in UC, while, in the stage of inflammation recurrence, it always appears accumulation, and dampness-heat qi blood accumulation in intestinal tract. That's why HPM which mainly contains monkshood shows a better effect for abdominal pain and diarrhea^[14].

Besides the properties of the partition herbs, the action mechanism of partitioned moxibustion also

relates to the thermal transmission from cone to the skin and then to the subcutaneous tissues. We JZ, et al consider that heat transfer process of indirect moxibustion from partition to the skin of points is mainly through the thermal conduction and thermal radiation. While, heat transfer from skin of points to the deep tissues even other region is mainly through the biological heat transfer effect^[18]. In addition, he that resonance radiation considers between moxibustion and acupoint infrared resonance radiation may be the foundation of the effect. Some researchers have pointed out that during the process of gingerpartitioned moxibustion, garlic-partitioned moxibustion and herb-partitioned moxibusiton, the light spectrum of moxibustion is the consistent with the normalized modified spectrum of human. Radiation peaks are almost in the vicinity of 7.5 µm, same as that in human body^[19-20]. This may be one of the common factors in HPM and GPM for the effect.

Experiment research of Zhao TP, et al point out that GPM can repair the colon injury by adjusting the sticky protein expression and promoting the mucus secretion in mucosal tissue^[21]. Wu HG, et al consider that the mechanism of HPM in treating the chronic UC may be by inhibiting and eliminating the expression of intestinal epithelial cell antigen, increasing T8⁺ cells number and function, and adjusting the proportion between T lymphocyte subsets to restore the colonic mucosa lesions^[16].

Moreover, partitioned moxibustion combines the triple functions of moxibustion, herbs and acupuncture points, and thus has good curative effect on immune regulation, anti-infection, improving microcirculation and many other aspects^[22].

Besides, the partitioned moxibustion is very effective, simple to use, and easy to promote. Especially GPM, bit's very convenient to get ginger. Most diseases are caused by spleen yang deficiency or weakness caused by improper diet, indulgence in cold food. Therefore, GPM is used to warm meridians and dispel cold, and dredge meridians and alleviate pain^[23].

GPM can well improve the abdominal pain, diarrhea, abdominal distention, and stomach distension. The two kinds of moxibustion are convenient, safe and effective. They can reduce the burden of intestines and stomach and also avoid the disadvantages of side effects of drugs. In the future research, we need to screen the effective disease and make standardized operation, so that the partitioned moxibustion can be easier to get popularized for keeping healthy and treating disease.

Conflict of Interest

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

Acknowledgments

This work was supported by National Natural Science Foundation of China (国家自然科学基金项目, No. 81173331, No. 81303033, No. 81473758); the 3-year Action Plan for Traditional Chinese Medicine of Shanghai Municipal Health Bureau (上海市卫生局中医药三年行动计划, No. ZYSNXD-CC-ZDYJ053); National Basic Research Program of China (973 Program, 国家重点基础研究发展计划, No. 2015CB554500); Innovation Program of Shanghai Municipal Education Commission (上海市教委科研创新项目, No. 2014YZ052).

Statement of Informed Consent

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

Received: 11 December 2015/Accepted: 15 January 2016

References

- Inflammatory Bowel Disease Branch of Gastroenterology of Chinese Medical Association. To standardize the diagnosis and treatment of inflammatory bowel disease in China consensus opinion. Gastroenterology, 2007, 12(8): 488-495.
- [2] Ye Y, Pang Z, Chen WC, Ju SW, Zhou CL. The epidemiology and risk factors of inflammatory bowel disease. Int J Clin Exp Med, 2015, 8(12): 22529-22542.
- [3] Zhang Q, Sha S, Xu B, Liang S, Wu K. Prevalence of colorectal cancer in patients with ulcerative colitis: A retrospective, multicenter study in China. J Cancer Res Ther, 2015, 11(4): 899-903.
- [4] Ashwin N. Environmental risk factors for inflammatory bowel diseases: a review. Dig Dis Sci, 2015, 60(2): 290-298.
- [5] Hua XG, Pan YY, Wu HG, Zhang LS, Zhang P. Observation on the effect of chronic nonspecific colitis by herbpartitioned moxibusiton. Modern Rehabilitation, 2000, 4 (8): 1250-1251.
- [6] Wu HG, Gao ZW, Zhang L. Clinical and experimental research on the effect of chronic nonspecific colitis by herb-partitioned moxibusiton. Zhongguo Zhen Jiu, 1992, 12(1): 28-31.
- [7] Wu HG, Wang JH, Chen HP, Zhang LD, Shi Z. Effect of herb-partitioned moxibustion in treating chronic ulcerative colitis and research on the colonic mucosal immunology. JCAM, 1995, 11(8): 20-23.
- [8] Inflammatory Bowel Disease Branch of Gastroenterology of Chinese Medical Association. To standardize the diagnosis and treatment of inflammatory bowel disease in China consensus opinion. Zhonghua Xiaohua Zazhi, 2007, 27(8): 545-550.

- [9] The spleen and stomach disease branch of Chinese Medical Association. Consensus of TCM diagnosis and treatment of ulcerative colitis. Zhonghua Zhongyiyao Zazhi, 2010, 25(6): 891-895.
- [10] State Administration of Traditional Chinese Medicine. Criteria of Diagnosis and Therapeutic Effects of Diseases and Syndromes in Traditional Chinese Medicine. Beijing: China Medical Science Press, 2002: 132-134.
- [11] Schroeder KM, Tremaine WJ, Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis: a randomized study. N Eng J Med, 1987, 317(26): 1625-1629.
- [12] Zhou L, Lu XH. Health-related quality of life of inflammatory bowel disease. Zhonghua Neike Zazhi, 2004, 43(5): 392-394.
- [13] Wu HG. Moxibustion. Shanghai: Shanghai Science and Technology Press, 2016: 200.
- [14] Wu HG, Shi Z, Zhu Y, Ma XP, Yao Y, Cui YH, Zhao TP, Liu HR. Clinical research on the effect of chronic nonspecific colitis by herb-partitioned moxibusiton. Shanghai Zhenjiu Zazhi, 2007, 26(4): 3-4.
- [15] Shi Z, Wu HG, Wang JH, Chen HP, Zhang LS. Effect of moxibustion in treating chronic ulcerative colitis and research on the colonic mucosal immunology. Shijie Huaren Xiaohua Zazhi, 2000, 8(21): 90-92.
- [16] Wu HG, Tan WL, Chen HP, Shi Z, Hua XG. Effect of moxibustion in treating chronic ulcerative colitis and research on the influence of the intestinal epithelial cells

- HLA-DR antigen. Zhen Ci Yan Jiu, 1999, 24(1): 12-16.
- [17] Sun TA, Ji J, Wu HG, Weng ZJ, Wu LY, Wang LD, Liu HR. Meta analysis for the treatment of ulcerative colitis by ginger-partitioned moxibusiton. 2014 Annual Conference of Clinical Chapter of China Association for Acupuncture and Moxibustion and the 21st National Acupuncture Clinical Academic Symposium Proceedings, 2014: 215-218.
- [18] Wei JZ, Shen XY, Ding GH, Zhao L. Analysis on the pathways and mechanism on warming regulation effect of material-partitioned moxibusiton. Zhongguo Zhen Jiu, 2007, 27(5): 391-393.
- [19] Yang HY, Xiao YC. Determination on the radiation characteristics of the near infrared spectrum of material-partitioned moxibusiton. Shanghai Zhenjiu Zazhi, 2003, 22 (9): 15-17.
- [20] Hong WX, Cai JH, Jing J. Research on the thermal radiation spectrum features of moxibustion. Yingyong Guangxue, 2004, 25(4): 1-3.
- [21] Zhao TP, Zhou S, Qin XD. Regulation on colonic mucosa sticky protein of UC rats of different moxibustion. Zhonghua Zhongyiyao Xuekan, 2010, 28 (8): 1590-1594.
- [22] Zhang M, Liu ZZ, Yang JM. The research status of moxibustion. Zhongyiyao Xuebao, 2015, 43(1): 73-77.
- [23] Xu YQ, Shang XK. The 11 years of clinical and experimental researches on material-partitioned moxibustion. Liaoning Zhongyiyao Daxue Xuebao, 2014, 11(3): 228-230.