JTCM 中医杂志 Journal of Traditional Chinese Medicine

Online Submissions: http://www.journaltcm.com
info@journaltcm.com

J Tradit Chin Med 2017 August 15; 37(4): 538-545
ISSN 0255-2922

RESEARCH ARTICLE

Effect of warming moxibustion Tianshu (ST 25, bilateral) and Qihai (CV 6) for the treatment of diarrhea-dominant irritable bowel syndrome: a patient-blinded pilot trial with orthogonal design

Yang Ling, Lu Yuan, Zhang Haifeng, Ma Xiaopeng, Bao Chunhui, Wu Huangan, Zhao Chen, Ding Guanghong, Qi Li, Zhou Shuang

Yang Ling, Lu Yuan, Ding Guanghong, Department of Mechanics and Engineering Science, Shanghai Key Laboratory of Acupuncture Mechanism and Acupoint Function, Fudan University, Shanghai 200433, China

Zhang Haifeng, Ma Xiaopeng, Bao Chunhui, Wu Huangan, Zhao Chen, Key Laboratory of Acupuncture-Moxibustion and Immunological Effects, Shanghai University of Traditional Chinese Medicine, Shanghai Research Institute of Acupuncture and Meridians, Shanghai 200030, China

Qi Li, E-Institute of Shanghai Municipal Education Committee, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China

Zhou Shuang, Department of Traditional Chinese Medicine, Changhai Hospital, Second Military Medical University, Shanghai 200433, China

Supported by the National Basic Research Program of China (973 Program): Research on Basic Theory and Regularity of Moxibustion (No. 2009CB522900); the National Natural Science Foundation of China: Involvement of Sigma-1 Receptor in Analgesic of Moxibustion on Chronic Visceral Hyperalgesia in Irritable bowel syndrome (IBS)-like Rats (No. 81303031); the National Natural Science Foundation of China: Study on the Mechanism of Moxibustion Effect on Reconstruction of Post Infectious (PI)-IBS Intestinal Homeostasis *via* Intestinal Microbiota-Mucosal Immunity (No. 81503656); Shanghai Key Laboratory of Acupuncture Mechanism and Acupoint Function: Effect of Needle Warming Moxibustion on Clinical Effect and Psychological Condition for Female D-IBS (No. 14DZ2260500); Shanghai Municipal Commission of Health and Family Planning: Observation on the Curative Effect and Ovarian Hormone Levels as Well as Psychological Condition of Female D-IBS Patients in Child-bearing Stage by Acupuncture & Moxibustion (No. 20164Y0151); the Shanghai Sailing Program: and the Mechanism of Central Response in the Treatment of Diarrhea-predominate Irritable Bowel Syndrome by Moxibustion (No. 15YF1411200)

Correspondence to: Prof. Zhou Shuang, Department of Traditional Chinese Medicine, Changhai Hospital, Second Military Medical University, Shanghai 200433, China. Zhoushuang8008@163.com; **Lu Yuan,** Department of Mechanics and Engineering Science, Shanghai Key Laboratory of Acupuncture Mechanism and Acupoint Function, Fudan University, Shanghai 200433, China. luyuan_sh@163.com

Telephone: +86-21-81871573

Accepted: February 10, 2017

Abstract

OBJECTIVE: To investigate the effects of warming moxibustion Tianshu (ST 25, bilateral) and Qihai (CV 6) in patients with diarrhea-dominant irritable bowel syndrome (D-IBS) by assessing predominant factors, and determining the best factor combinations and their interactions. To identify the optimal quantity of warming moxibustion Tianshu (ST 25, bilateral) and Qihai (CV 6) to achieve optimal efficacy.

METHODS: An L9 (3^4) orthogonal design was applied to 233 confirmed subjects based on the three most influential factors and the three most frequently used levels. Nine programs were designed. Subjects were assigned to four subgroups according to age and gender; each subject underwent one of the nine programs randomly. We selected Tianshu (ST 25, bilateral) and Qihai (CV 6). The scores of symptoms and the IBS Quality of Life (IBS-QOL) were evaluated after the final treatment.

RESULTS: After treatment, clinical symptoms of all patients were significantly improved ($P = 0.001$). Quality of life also improved significantly ($P < 0.05$). For all the participants, frequency was the dominat-

ing factor regarding symptoms (P = 0.01). Duration was the dominating factor for quality of life (P = 0.0001). The best combination for improving symptoms in 30-40-year-old male and female patients was two courses of 10 min each once a day, and for 41-50-year-old male and female patients it was three courses of 10 min (males) or 30 min (females) twice a day. The best combination for quality of life was three courses of 20 min once a day. No interaction was found between frequency and course, or frequency and duration.

CONCLUSION: Warming moxibustion Tianshu (ST 25, bilateral) and Qihai (CV 6) is a promising therapy for D-IBS. To acquire optimal efficacy, the three main factors (duration, frequency and treatment course) of the warming moxibustion should reach a specific quantity and be combined appropriately.

Keywords: Irritable bowel syndrome; Diarrhea; Warming moxibustion; Point ST25 (Tianshu); Point CV6 (Qihai); Quality of life

INTRODUCTION

Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder characterized by intermittent or persistent abdominal pain or discomfort, altered bowel habits, and abnormal bowel characteristics.[1-3] Population prevalence rates vary widely.[4-6] A recent population-based investigation showed that the estimated prevalence of IBS is around 11.2%.[7,8] IBS results in a poor quality of life,[9] high rates of absenteeism, high health care utilization[10] and imposes a substantial economic burden of high direct and indirect productivity costs.[11]

Warming moxibustion (WM) is a traditional treatment based on the theories of Traditional Chinese Medicine. It mediates its effects using mainly the heat of burning moxa to stimulate acupoints. We reported that WM is a promising therapy for diarrhea-dominant irritable bowel syndrome (D-IBS) and relies on an appropriate stimulus quantity.[12-14] Treatment frequency, duration and course are the three most influential factors that contribute to the quantity and effect of moxibustion according to years of clinical observation.

An orthogonal study design is used when a process is affected by several different factors, and is achieved by matching each level of each factor with an equal number of each level of the other factors. There have been no orthogonal designs applied to studies of IBS.[15-18]

Although clinical and animal studies of IBS have been performed with moxibustion, the most effective quantity of WM still remains unknown.[12-14,19] This study determined how to determine the most effective quantity for the best effect, which were the predominant factors influencing the effect of moxibustion, which levels are the best and what is the perfect combination of factors.

MATERIALS AND METHODS

Study design

This study was a two-center, randomized, patient-blinded pilot clinical trial to evaluate the efficacy of moxibustion for D-IBS. The trial is registered at Controlled Clinical Trials: ChiCTR-TNRC-10000883. It preliminarily screened predominant factors and the best combination of factors and levels for warming moxibustion Tianshu (ST 25, bilateral) and Qihai (CV 6) (WM) for the treatment of D-IBS. We selected the three most commonly used levels of frequency, duration, and courses of treatment in clinical practice and matched the nine different resulting programs. The L9 (3^4) orthogonal design was applied to the evaluation of the regularity of moxibustion quantity in patients of different ages and genders. The three main influential factors and their three most frequently used levels were identified (Table 1) for a total of nine different programs. Each of the nine treatment programs was repeated six times.

The prevalence of IBS was higher for women compared with men and lower for individuals older than 50 years in the general population.[8,9] In contrast, a previous study reported that in many Eastern countries including China, no female predominance among IBS patients was observed.[20] The prevalence of IBS in women is most common between late teenage to mid-forties,[8,21] and for males it is between the ages of 20-70 years.[22,23] Therefore, we set an age of 30-50 years as the inclusion criteria. To maintain homogeneity of the orthogonal design, all patients were divided into four subgroups according to gender and age. The sample size was calculated according to the third version of the statistical package of the Medical Statistics chapter of the Chinese Medical Encyclopedia PEMS 3.1 for Windows.

Table 1 Three factors and their three levels of warming moxibustion

Level	Frequency	Duration (min)	Treatment course
1	Once every two days	10	1
2	Once a day	20	2
3	Twice a day	30	3

Random method

SPSS 13.0 (SPSS Inc., Chicago, IL, USA) was used to generate random numbers, and a sealed envelope was used to assign subjects randomly to one of the nine treatments by assistant physicians according to their visit orders.

Subjects and ethical approval

A total of 233 patients with confirmed D-IBS were recruited from the Shanghai Research Institute of Acupuncture and Meridian, Central Hospital of Jiading District of Shanghai from 2008 to 2011, through newspaper, hospital website, and bulletin boards. All subjects gave written informed consent at the beginning of the trial and were free to withdraw from the study at any time. The study was approved by the local ethics committee.

Inclusion criteria

(a) Meet the Rome Ⅲ diagnostic criteria;[24-26] (b) 30-50 years old, no gender limits; and (c) have not accepted any other treatment recently and is compliant.

Exclusion criteria

(a) Nonfunctional intestinal diseases; (b) severe diseases such as cerebral vessel diseases, liver or kidney diseases; and (c) mental disorders, pregnancy, or lactation.

WM protocol

Tianshu (ST 25, bilateral) and Qihai (CV 6) were selected according to the Nomenclature and Location of Acupuncture Points (GB/T12346-2006).[27] One end of the purifying moxa stick (18 mm × 200 mm; Henan Nanyang Moxa Biological Products Co., Ltd., Henan Province, PR China) was ignited. The distance between the ignited moxa stick and skin was approximately 2 cm. Patients should feel heat that should not burn. Treatments were given according to the programs listed in Table 2 by a physician who had more than three years of moxibustion experience. Each moxibustion session lasted 6 days, and 1-day intervals were set between sessions.

Outcome measures

The primary outcome was a change in symptom score from baseline after WM treatment. Symptom scores were determined according to the criteria of diagnosis and therapeutic effects for clinical diseases and syndromes.[28] It was assessed by a modified gastrointestinal symptom questionnaire. The criteria had three levels: (a) markedly effective: normal defecation with alleviation of other syndromes, R (change rate of symptom score) ≥ 70%; (b) effective: substantially decreased frequency of defecation with improvement in other syndromes, 30% ≤ R ≤ 70% ; and (c) ineffective: no change in frequency of defecation or other syndromes, R < 30%.

The secondary outcome was quality of life as assessed by irritable bowel syndrome quality of life (IBS-QOL).[29,30]

Statistical analysis

Analyses were performed using SPSS 13.0 (SPSS Inc., Chicago, IL, USA). Mean ± standard deviation ($\bar{x} \pm s$) were used to describe continuous variables and proportions for categorical data. Differences in means among groups were compared by one-way analysis of variance (ANOVA), the least significant differences test (LSD), and Games-Howell test separately when appropriate. Differences in means within groups were compared using the paired-samples *t*-test. Wilcoxon's nonparametric test and the two-related-samples test were performed when there was a heterogeneity in variance. Enumeration data were assessed by the χ^2 test or signed rank sum test. A P value < 0.05 was considered statistically significant.

RESULTS

Subjects

Seventeen patients were lost because of the following reasons: business trip (n = 3), pregnancy (n = 1), other medications (n = 6), allergy to WM (itch-

Table 2 List of programs

Group	Frequency	Duration (min)	Treatment course
First program	Once every two days	10	1
Second program	Once every two days	20	2
Third program	Once every two days	30	3
Fourth program	Once a day	10	3
Fifth program	Once a day	20	1
Sixth program	Once a day	30	2
Seventh program	Twice a day	10	2
Eighth program	Twice a day	20	3
Ninth program	Twice a day	30	1

iness around the points) (n = 1), and unknown reason (n = 6). The rate of loss was 7%. Finally, there were 216 patients completed the treatment course (Figure 1). The baseline characteristics of patients in the four subgroups were not statistically different (P > 0.05).

Clinical efficacy

Clinical symptoms in different programs showed significant improvement after treatment (P = 0.001) (Table 3). There was a significant difference in the total effective rate among the three levels of frequency (χ^2 = 7.187, P = 0.027). Nonparametric tests indicated that level 2

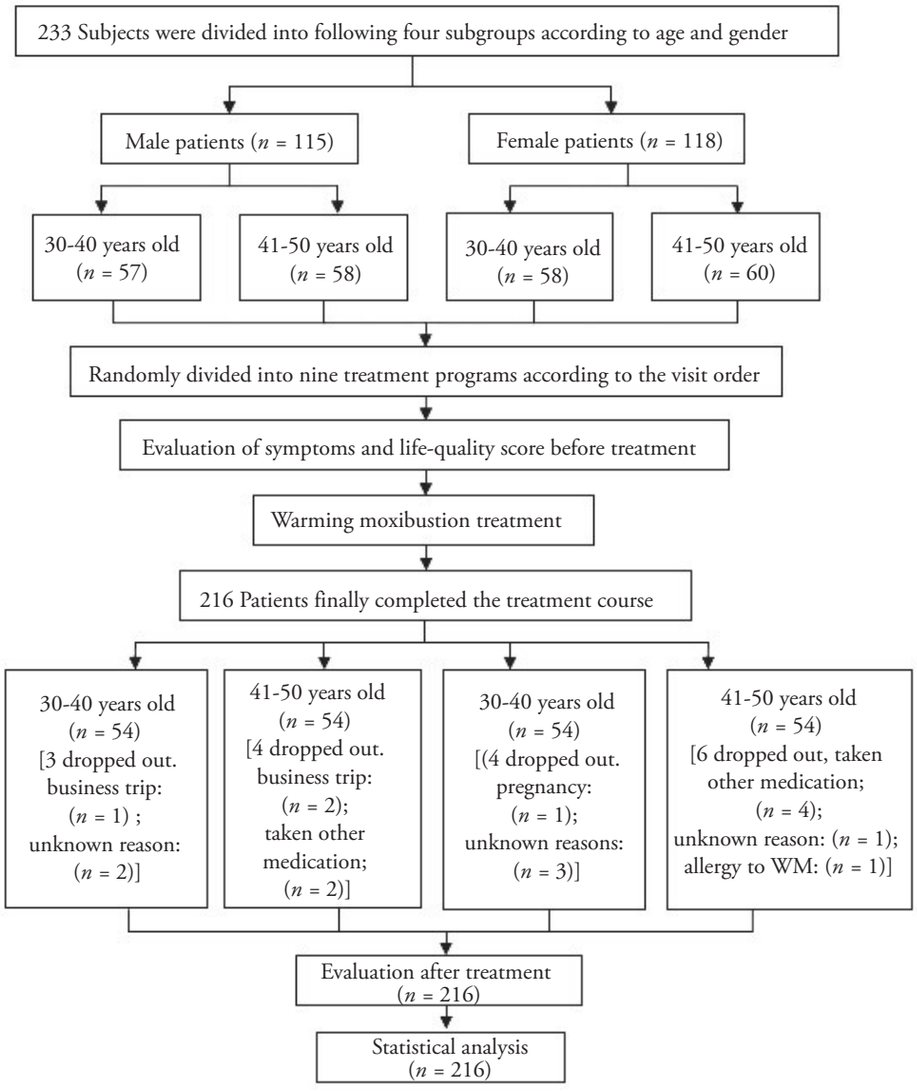

Figure 1 Flow chart of the study protocol

Table 3 Improvement of clinical symptom score after warming moxibustion treatment ($\bar{x} \pm s$)

Age (years)	Gender/n	Symptom score		t value	P value
30-40	Male/54	Before treatment	27±8	14.650	0.001
		After treatment	10±8		
	Female/54	Before treatment	23±6	13.002	0.001
		After treatment	11±7		
41-50	Male/54	Before treatment	26±11	12.203	0.001
		After treatment	14±9		
	Female/54	Before treatment	29±10	14.884	0.001
		After treatment	12±8		
All patients in the study 216		Before treatment	26±9	26.388	0.001
		After treatment	12±8		

(once a day) was better than level 1 (once every two days) (P = 0.008). There was no statistical difference between the three levels of duration and treatment courses (Table 4). The IBS-QOL in the different programs improved significantly after treatment (P < 0.05) (Table 5).

Dominating factors

The data of 41-50-year-old male patients is used as an example. For the reason of limited space, the rest of the data is not shown.

ANOVA indicated statistical significance among the three levels of the three factors in terms of differences in the scores for clinical symptoms (P = 0.042). Frequency was the dominating factor in improving symptoms of 41-50-year-old male patients, and twice a day was the best frequency (Table 6).

The other results are shown in Table 7. For 30-40-year-old male patients, there was no difference among the three factors with regard to improving symptoms or IBS-QOL. For female patients in the 30-40 and 41-50-year-old groups, duration was the dominating factor for IBS-QOL (P = 0.037, P = 0.015).

For all the patients in the study, ANOVA results indicated that frequency was the dominating factor among the three levels of the three factors in terms of symptom improvement (P = 0.01). Duration was the dominating factor for IBS-QOL (P = 0.0001).

Interaction of frequency and duration

There was no statistical significance between the frequency and duration in terms of improving symptoms and IBS-QOL in patients of different age and gender. These results indicated that frequency and duration may have separate roles.

Best combination

Comparison of the K value indicated that the best combination for improving symptoms of 41-50-year-old male patients was three treatment courses of 10 min twice a day. To improve the IBS-QOL, the best combination was three treatment courses of 20 min once a day (Table 8, 9). The four subgroups results are shown in Table 10.

DISCUSSION

WM requires a proper stimulus quantity to achieve effective results. Efficacy is influenced by several factors. Ancient practitioners performed WM based on gender,

Table 4 Effective rates among levels and factors [*n* (%)]

Factor	Level	*n*	Marked effective	Effective	Ineffective	Total effective rate	χ^2 value	*P* value
Frequency	Once every two days	72	15 (20.8)	43 (59.8)	14 (19.4)	58 (80.6)	7.187	0.027
	Once a day	72	31 (43.1)	32 (44.4)	9 (12.5)	63 (87.5)		
	Twice a day	72	22 (30.6)	36 (50.0)	14 (19.4)	58 (80.6)		
Duration (min)	10	72	20 (27.8)	37 (51.4)	15 (20.8)	57 (79.2)	1.557	0.459
	20	72	26 (36.1)	35 (48.6)	11 (15.3)	61 (84.7)		
	30	72	22 (30.6)	40 (55.6)	10 (13.8)	62 (86.2)		
Treatment course	1	72	15 (20.8)	38 (52.8)	19 (26.4)	53 (73.6)	6.955	0.182
	2	72	24 (33.3)	36 (50.0)	12 (16.7)	60 (83.3)		
	3	72	26 (36.1)	37 (51.4)	9 (12.5)	63 (87.5)		

Table 5 Improvement of life quality score after warming moxibustion treatment ($\bar{x} \pm s$)

Age (years)	Gender/*n*	Quality of life score		*t* value	*P* value
30-40	Male/54	Before treatment	64±20	5.061	0.001
		After treatment	56±17		
	Female/54	Before treatment	69±20	2.582	0.013
		After treatment	64±19		
41-50	Male/54	Before treatment	69±20	5.065	0.001
		After treatment	60±16		
	Female/54	Before treatment	86±25	6.115	0.001
		After treatment	72±20		
All patients in the study 216		Before treatment	72±23	9.298	0.001
		After treatment	63±19		

Table 6 ANOVA results of differences in scores for clinical symptoms and quality of life among the three levels of the three factors of 41-50-year-old male patients

Index		SS	df	MS	*F* value	*P* value
Difference of score evaluation for clinical syndromes	Total aberrance	10496.000	54	-	-	-
	A	330.2000059	2	165.130	3.384	0.042
	B	93.481	2	46.741	0.958	0.391
	C	50.815	2	25.407	0.521	0.597
	Error	2293.370	47	48.795	-	-
Difference of score evaluation for life quality	Total aberrance	15234.000	54	-	-	-
	A	69.148	2	34.574	0.175	0.840
	B	781.370	2	390.685	1.982	0.149
	C	151.370	2	75.685	0.384	0.683
	Error	9263.148	47	197.088	-	-

Notes: ANOVA: analysis of variance; SS: standard deviation square; df: degree of freedom; MS: mean square; A: frequency; B: duration; C: treatment course.

Table 7 Predominant factors of symptoms and quality of life in four subgroups

Subgroup	Symptom	Quality of life
30-40 year old male	None	None
30-40 year old female	None	Duration
41-50 year old male	Frequency	None
41-50 year old female	None	Duration
All patients in the study	Frequency	Duration

ture and moxibustion,[31-35] but none have reported the most effective quantity of moxibustion.

Duration

In a study by Bai,[36] prolonged moxibustion increased the immediate analgesic and postanalgesic effects. However, no direct relationship was found between duration and effect of moxibustion; the pain threshold was gradually reduced when the duration of moxibustion

Table 8 Comparison of differences in scores for clinical symptoms and quality of life among the three levels of the three factors in 41-50-year-old male patients

Sequence	Level			Difference of symptom							Difference of life quality						
				1	2	3	4	5	6	Total	1	2	3	4	5	6	Total
1	1	1	1	4	4	6	9	15	7	45	6	0	0	8	6	0	20
2	2	2	2	13	6	1	16	12	8	56	3	49	12	16	34	1	115
3	3	3	3	14	0	5	12	7	18	56	15	10	-7	9	8	-7	28
4	1	2	3	12	9	21	8	10	13	73	36	-5	2	-6	5	38	70
5	2	3	1	12	1	3	10	15	14	55	25	-2	-1	3	1	20	46
6	3	1	2	24	13	11	12	19	17	96	4	2	8	6	10	8	38
7	1	3	2	19	7	7	10	7	18	68	15	0	-4	-5	1	19	26
8	2	1	3	39	14	9	8	13	22	105	12	1	37	4	28	26	108
9	3	2	1	33	15	5	10	11	18	92	41	-10	7	-6	5	30	67

Table 9 Orthogonal design results of clinical symptoms and quality of life among the three levels of the three factors in 41–50-year-old male patients

Value	Difference of symptom			Difference of life quality		
	A	B	C	A	B	C
K1	186	246	192	192	166	133
K2	216	221	220	269	252	179
K3	244	179	234	133	100	206

Notes: the best combination for improving the symptoms of 41-50-year-old male patients was A3B1C3: three treatment courses of 10 min twice a day. To improve the quality of life, the best combination was A2B2C3: three treatment courses of 20 min once a day. A: frequency; B: duration; C: treatment course.

age, disease, constitution, and season. Many studies have investigated the treatment of IBS with acupunc-

was longer than 20 min. Our results are not fully consistent with those of Bai in terms of the relationship be-

Table 10 The best combination for symptoms and life quality improvement in four subgroups

Subgroup	Symptom improvement	Life quality improvement
30-40 year old male	Once a day, 10 min, 2 courses	Once a day, 20 min, 3 courses
30-40 year old female	Once a day, 10 min, 3 courses	
41-50 year old male	Twice a day, 10 min, 3 courses	
41-50 year old female	Twice a day, 30 min, 3 courses	
All patients in the study	Once a day, 20 min, 1 course	

tween duration and efficacy. Our study showed that clinical efficacy was not always increased with a prolonged duration of moxibustion. Therefore, the most effective treatment requires a proper stimulus quantity based on patient age, gender, and symptoms. This is also in concordance with theories of ancient physicians about the proper stimulus quantity of moxibustion.

Frequency

This study revealed that frequency was the predominant factor in improving clinical syndromes for all subjects and for 41-50-year-old male patients, twice a day was optimal. This study showed that twice a day was the best frequency with which to influence many indices and indicated that a higher frequency was more effective at improving clinical syndromes. We found no interactions between frequency and duration for the improvement of all syndromes, which indicated that frequency and duration may have separate roles.

Treatment course

This study attempted to determine the influence of treatment course on WM by evaluating three levels of treatment course (6, 12, and 18 days). The effective rate among all three levels improved significantly after treatment, which revealed a relationship between the effect and different levels of WM courses for the improvement of clinical symptoms. Consistent with our assumption, a longer treatment course was more likely to produce a greater effect.

Analysis of the best program

In this study, two courses of 10 min each time once a day was the best combination for the improvement of clinical symptoms in 30-40-year-old male and female patients, while three courses of 10 min (males) or 30 min (females) twice a day was the optimal combination for 41-50-year-old male and female patients. Thus, for younger patients, a lower frequency and shorter treatment course improved symptoms, whereas older patients required a higher frequency and longer treatment course to obtain an optimal effect. This suggests that young patients may have stronger immunity, and thus respond to WM more sensitively. For all subjects, three courses of 20 min once a day was the optimal combination for improved IBS-QOL.

No interaction between frequency and duration was found, but the predominant factors for different indices of different ages and genders of patients with D-IBS were identified. These results should help guide clinical practice. However, this study only enrolled Chinese subjects; therefore further studies of different ethnic groups are required.

In conclusion, our findings suggest that warming moxibustion Tianshu (ST 25, bilateral) and Qihai (CV 6) improved clinical symptoms and quality of life of IBD patients. To acquire optimal efficacy, the three main factors (duration, frequency and treatment course) of warming moxibustion should reach a specific quantity and be combined appropriately.

ACKNOWLEDGEMENT

The authors thank Edanz for language editing.

REFERENCES

1 **Videlock EJ**, Chang L. Irritable bowel syndrome: current approach to symptoms, evaluation, and treatment. Astroenterol Clin North Am 2007; 36(3): 665-685.

2 **Drossman DA**. The functional gastrointestinal disorders and the Rome Ⅲ process. Gastroenterology 2006; 130(5): 1377-1390.

3 **Camilleri M**. Peripheral mechanisms in irritable bowel syndrome. N Engl J Med 2013; 368(6): 578-579.

4 **Hungin AP**, Whorwell PJ, Tack J, Mearin F. The prevalence, patterns and impact of irritable bowel syndrome: an international survey of 40 000 subjects. Aliment Pharmacol Ther 2003; 17(5): 643-650.

5 **Naeem SS**, Siddiqui EU, Kazi AN, Memon AA, Khan ST, Ahmed B. Prevalence and factors associated with irritable bowel syndrome among medical students of Karachi, Pakistan: A cross-sectional study. BMC Res Notes 2012; 5(1): 255.

6 **Valerio-Ureña J**, Vásquez-Fernández F, Jiménez-Pineda A, et al. Prevalence of irritable bowel syndrome in Veracruz City, Mexico: A community-based survey. Rev Gastroenterol Mex 2010; 75(1): 36-41.

7 **Lix Lisa M**, Yogendran Marina S, Shaw Souradet Y, Targownick Laura E, Jones J, Bataineh O. Comparing administrative and survey data for ascertaining cases of irritable bowel syndrome: a population-based investigation. BMC Health Services Research 2010; 1(10): 31.

8 **Lovell RM**, Ford AC. Global prevalence of and risk factors for irritable bowel syndrome: a Meta-analysis. Clin Gastroenterol Hepatol 2012; 10: 712-721.

9 **Soares RL**. Irritable bowel syndrome: a clinical review. World J Gastroenterol 2014; 20(34): 12144-12160.

10 **Makharia GK**, Verma AK, Amarchand R, et al. Prevalence of irritable bowel syndrome: a community based study from northern India. J Neurogastroenterol Motil 2011; 17(1): 82-87.

11 **Doshi JA**, Cai Q, Buono JL, et al. Economic burden of irritable bowel syndrome with constipation: a retrospective analysis of health care costs in a commercially insured population. J Manag Care Pharm 2014; 20: 382-390.

12 **Wu HG**, Jiang B, Zhou EH, et al. Regulatory Mechanism of electro-acupuncture in irritable bowel syndrome: preventing MC activation and decreasing SP VIP secretion. Dig Dis Sci 2008; 53(6): 1644-1651.

13 **Zhou EH**, Liu HR, Wu HG, et al. Suspended moxibustion relieves chronic visceral hyperalgesia *via* serotonin pathway in the colon. Neurosci Lett 2009; 451(2): 144-147.

14 **Zhou EH**, Liu HR, Wu HG, et al. Herb-partition moxibustion relieves chronic visceral hyperalgesia and 5-HT concentration in colon mucosa of rats. Neurol Res 2009; 31(7): 734-737.

15 **Bensoussan A**, Talley Nick J, Hing Michael, et al. Treatment of irritable bowel syndrome with Chinese herbal medicine, a randomized controlled trial. JAMA 1998; 280 (18): 1585-1589.

16 **Mark Pimentel**, Anthony Lembo, Chey William D, et al. Rifaximin therapy for patients with irritable bowel syndrome without constipation. N Engl J Med 2011; 364(1): 22-32.

17 **Camilleri M**, Northcutt AR, Kong S, Dukes GE, McSorley D, Mangel AW. Efficacy and safety of alosetron in women with irritable bowel syndrome: a randomised, placebo-controlled trial. Lancet 2000; 355(9209): 1035-1040.

18 **Ritchie JA**, Truelove SC. Treatment of irritable bowel syndrome, with lorazepam, hyoscine butylbromide, and ispaghula husk. Br Med J 1979; 1(6160): 376-378.

19 **Anastasi JK**, McMahon DJ, Kim GH. Symptom management for irritable bowel syndrome, a pilot randomized controlled trial of acupuncture/moxibustion. Gastroenterol Nurs 2009; 32(4): 243-255.

20 **Gwee KA**, Lu CL, Ghoshal UC. Epidemiology of irritable bowel syndrome in Asia: something old, something new, something borrowed. J Gastroenterol Hepatol 2009; 24 (10): 1601-1607.

21 **Mulak A**, Taché Y, Larauche M. Sex hormones in the modulation of irritable bowel syndrome. World J Gastroenterol 2014; 20(10): 2433-2448.

22 **García Rodríguez LA**, Ruigómez A, Wallander MA, Johansson S, Olbe L. Detection of colorectal tumor and inflammatory bowel disease during follow-up of patients with initial diagnosis of irritable bowel syndrome. Scand J Gastroenterol 2000; 35(3): 306-311.

23 **Henry CL**. Small intestinal bacterial overgrowth, a framework for understanding irritable bowel syndrome. JAMA 2004; 292(7): 852-858.

24 **Longstreth GF**, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. Gastroenterology 2006; 130(5): 1480-1491.

25 **Videlock EJ**, Chang L. Irritable bowel syndrome: current approach to symptoms, evaluation, and treatment. Gastroenterol Clin North Am 2007; 36(3): 665-685.

26 **Khan Sarah**, Chang Lin. Diagnosis and management of IBS. J Gastroenterol Hepatol 2010; 7(10): 565-581.

27 General Administration of Quality Supervision, Inspection and Quarantine of the People's Republic of China, Standardization Administration of the People's Republic of China. Nomenclature and Location of Acupuncture Points (GB/T 12346-2006). Beijing: Standards Press of China, 2006: 11-36.

28 **Sun Chuanxing**. Criteria of diagnosis and therapeutic effects for clinical diseases and syndromes. 2nd ed. Beijing: People's Military Medical Press, 1998: 79.

29 **Drossman DA**, Patrick DL, Whitehead WE, et al. Further validation of the IBS-QOL: A disease-specific quality-of-life questionnaire. Am J Gastroenterol 2000; 95(4): 999-1007.

30 **Huang WW**, Zhou FS, Bushnell DM, Diakite C, Yang XH. Cultural adaptation and application of the IBS-QOL in China: a disease-specific quality-of-life questionnaire. Qual Life Res 2007; 16(6): 991-996.

31 **Forbes A**, Jackson S, Walter C, Quraishi S, Jacyna M, Pitcher M. Acupuncture for irritable bowel syndrome: a blinded placebo controlled trial. World J Gastroenterol 2005; 11(26): 4040-4044.

32 **Schneider A**, Enck P, Streitberger K, et al. Acupuncture treatment in irritable bowel syndrome. Gut 2006; 55(5): 649-654.

33 **Manheimer E**, Wieland LS, Cheng K, et al. Acupuncture for treatment of irritable bowel syndrome: systematic review and Meta-analysis. Am J Gastroenterol 2012; 107(6): 835-847.

34 **Rohrbock RB**, Hammer J, Vogelsang H, Talley NJ, Hammer HF. Acupuncture has a placebo effect on rectal perception but not on distensibility and spatial summation: a study in health and IBS. Am J Gastroenterol 2004; 99 (10): 1990-1997.

35 **Xiao WB**, Liu YL. Rectal hypersensitivity reduced by acupoint TENS in patients with diarrhea-predominant irritable bowel syndrome: a pilot study. Dig Dis Sci 2004; 49 (2): 312-319.

36 **Bai YH**. Animal experiment on time-effect and quantity-effect of moxibustion analgesia. Shanghai Zhong Yi Yao Yan Jiu Xue Bao 1998; 12(1): 54-58.