Ba-Duan-Jin alleviates pain and fibromyalgia-related symptoms in patients with fibromyalgia: results of a randomised controlled trial

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Abstract

Objective

Fibromyalgia is a chronic debilitating pain syndrome. There has been growing interest in the development of non-pharmacological therapies. Ba-Duan-Jin is an ancient Chinese exercise for health promotion, yet easy to learn. The purpose of this study is to evaluate the effectiveness of Ba-Duan-Jin in managing fibromyalgia symptoms experienced by Chinese patients.

Methods

In this randomised, usual therapy-controlled study, patients with fibromyalgia practiced Ba-Duan-Jin for one hour, twice a week for 12 weeks. The primary outcome measure was change in the Visual Analogue Scale for pain (pain VAS). Secondary outcomes included the Fibromyalgia Impact Questionnaire (FIQ), the Multidimensional Assessment of Fatigue (MAF), the Pittsburgh Sleep Quality Index (PSQI), the Beck Depression Inventory (BDI), the Perceived Stress Scale (PSS), and the Tender Point Count (TPC). These measures were assessed at baseline and after 4, 8, and 12 weeks. The Patient Global Impression of Change (PGIC) was collected at week 12. The Mann-Whitney U-test was performed using the intention-to-treat population.

Results

A total of 62 fibromyalgia patients were randomised to the Ba-Duan-Jin or the control groups. For the Ba-Duan-Jin group, significant improvement in pain VAS, FIQ, MAF, PSQI, and TPC were documented at weeks 4 ($p \leq 0.046$) and continued at week 8 ($p \leq 0.003$). At week 12, all of the outcome measures including BDI and PSS exhibited significant improvement ($p \leq 0.004$), and PGIC ratings were significantly better ($p < 0.001$). No significant changes in the control group were observed.

Conclusion

This study suggests that Ba-Duan-Jin exercise has the potential to be a valuable non-pharmacological intervention among Chinese fibromyalgia patients.

Key words

fibromyalgia, Qigong, pain management

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Introduction

Fibromyalgia is a clinical syndrome characterised by chronic widespread musculoskeletal pain, disordered sleep, and fatigue (1). This condition affects up to 5% of the general population globally, making it the second most common rheumatologic condition, trailing only osteoarthritis (2). Recent literature shows that genetics play an important role in the development of fibromyalgia (3).

The role that pharmacological therapy plays in the care of fibromyalgia patient varies considerably by world region and/or country. In the United States, three medications (pregabalin, duloxetine, and milnacipran) have been approved by the Food and Drug Administration (FDA) to treat fibromyalgia. By contrast, the European Medicines Agency has not approved any medication for this indication. Only about half of the fibromyalgia patients treated with any one of the FDA-approved medications benefit considerably from its use, a nearly equal number derive little or no benefit from taking these medications (4). Additional barriers to the use of these drugs include their moderately high cost and their potential for causing adverse effects (5). Observations such as these prompted the European League Against Rheumatism (EULAR) to advise that these medications be reserved for fibromyalgia patients with severe pain and/or very troublesome sleep disturbance (6).

There is a clear need for more efficacious and cost-effective therapies to manage the symptoms of fibromyalgia (7). Four recent guidelines from Europe, Canada, Israel and Germany agree that fibromyalgia therapy should be tailored to the individual patient and that non-pharmacological interventions should be considered as the first-line of therapy in most cases (6, 8). Among these non-pharmacological interventions for fibromyalgia, exercise is recommended as the best method to achieve improvement in pain and physical function.

Chinese Qigong (pronounced "che-gong") is a generic term for a centuries-old category of Chinese fitness exercise that has been referred to as 'meditative movement' (9). Such exercise practices include Tai Chi (太极), Ba-Duan-Jin (八段锦), Yi-Jin-Jing (易筋经), Wu-Qin-Xi (五禽戏), and Liu-Zi-Jue (六字诀), to name a few. Although the exact methods and relative rigors of these exercises differ, they all exhibit health-promoting effects, evidenced by centuries of practice by Chinese people and are now recommended for that purpose by Chinese physicians. Tai Chi is probably the Qigong that is best known in western countries. It offers recognised benefits in rehabilitation medicine (10) and has proven benefits for patients with fibromyalgia (11). It was, thus, interesting to explore whether other forms of Chinese Qigong exercise could also prove to be beneficial for patients with fibromyalgia.

The original Chen style of Tai Chi, from the 16th century, was most likely developed for the purpose of martial arts combat training, with the ultimate goal to perpetuate the Chen family dynasty (12). In its long form Tai Chi has had 108 movements, but in modern times that number has been reduced to only 37 movements. By contrast, Ba-Duan-Jin was originally designed as a simpler form of exercise specifically for the purpose of medical therapy. With only 8 essential movements, Ba-Duan-Jin is easier to learn than Tai Chi and more likely to achieve compliance among patients with rehabilitation potential.

Also known as Baduanjin, Eight Brocades, or Eight-Section Brocade, Ba-Duan-Jin, is a common form of "self-health-care" Qigong exercise that has been practiced by Chinese people for at least eight hundred years. It consists of eight sets of simple movements. By combining meditation with slow, graceful movements, deep breathing, and relaxation, Ba-Duan-Jin practitioners believe it has the ability to move vital energy (Qi) throughout the body. Ba-Duan-Jin is also considered to be a multicomponent intervention that integrates physical, psychosocial, emotional, spiritual, and behavioral elements. While the biological mechanisms remain unclear, previous clinical trials have demonstrated that Ba-Duan-Jin can improve sleep quality (13), physical health (14), and mental health (15) in patients with various chronic dis-

eases. In addition, several systematic reviews have indicated that Ba-Duan-Jin might be beneficial in other medical conditions, including hypertension (16) and hyperlipidemia (17).

Since Ba-Duan-Jin is a simple patterned exercise, it is easy to learn and is gentle on the body. For that reason, the authors predicted that it may be ideally suited as a non-pharmacological therapy for patients with the fibromyalgia syndrome. The main objective of the current study was to investigate the efficacy of Ba-Duan-Jin for Chinese patients with fibromyalgia. Any benefit of Ba-Duan-Jin observed in a Chinese population could then be extrapolated for study among fibromyalgia patients from other parts of the world, and with other ethnic backgrounds.

Methods

Study participants

The trial was conducted from March 2015 through February 2017 at Guang'anmen Hospital, a tertiary research hospital in Beijing, China. The study protocol was approval by the ethics committee of the hospital (approval number 2014EC079-02). The study candidates were patients who visited the outpatient rheumatology clinic for body pain and/or were previously given a diagnosis of fibromyalgia syndrome. To be eligible, patients had to meet the 1990 American College of Rheumatology (ACR) Research Classification Criteria for fibromyalgia (18), and be between the ages of 18 to 70 years of age. All recruited participants signed a written informed consent.

Otherwise eligible patients were excluded if they had practiced Ba-Duan-Jin, Tai Chi, yoga, or other forms of Qigong exercise within 12 months of their recruitment to the study. Patients were excluded if they had dementia, cancer, or other serious medical conditions that might confound the study's results. Other exclusions included: 1. any poorly-controlled comorbid medical conditions, such as thyroid disease, inflammatory arthritis, systemic lupus erythematosus, rheumatoid arthritis, myositis, vasculitis or Sjögren's syndrome; 2. pregnancy or planned pregnancy within the study period; or 3. patients residing more than 70 miles from the research site.

Study design

The study design was randomised and usual therapy-controlled. The randomisation scheme was generated by computer using the SAS system (v. 5.2.127 for Windows, and using blocked randomisation with a block size of 10). Eligible participants were randomly assigned to the Ba-Duan-Jin group or to the control group, with 1:1 ratio. Each participant had his or her own unique code number sealed in sequentially-numbered, opaque envelopes and kept in the scientific research office of the hospital, so it would be unknown by the study investigators and the participants. Participants in both groups received one-hour of fibromyalgia education prior to any other study intervention. During that session, they were all instructed to continue taking, throughout the study, any stable pre-study medication(s) that they had already taken for at least one-month.

Interventions

- *Ba-Duan-Jin intervention*.

Guided by a physician, the participants met twice weekly, for 12 weeks, in the outpatient section of the hospital, to participate in an hour-long, supervised group Ba-Duan-Jin exercise. During the first exercise session, participants learned about the history and principles of Ba-Duan-Jin. Each participant was given an instructional handout and video showing an instructor performing Ba-Duan-Jin. All subsequent sessions, each led by a physician, began with a brief review of the Ba-Duan-Jin movements, breathing and relaxation techniques, followed by a warm-up session leading into repetition of the eight forms of Ba-Duan-Jin (see the supplementary material: Essentials of Ba-Duan-Jin). Participants were encouraged to practice Ba-Duan-Jin daily at home, by following the movements shown on the video. Each Ba-Duan-Jin home practice session took about 16 minutes to complete.

- *Control intervention*. Participants in the control group were self-assessed similarly to those in the Ba-Duan-Jin group and were instructed to continue their stable usual therapy. After completion of this study, following the 12-week assessment, the participants in the control group were invited to practice supervised in-group Ba-Duan-Jin exercise for 12 weeks.

Outcome measures

In this study, the participants were self-assessed regarding the severity of various fibromyalgia symptoms, including pain, fatigue, sleep dysfunction, depression, anxiety, and quality of life. The primary outcome measure was the visual analogue scale (VAS) for pain (pain VAS, range, 0 to 100 mm, where higher scores indicated the perceived pain to be more severe) (19). Secondary outcome measures included the following: the Fibromyalgia Impact Questionnaire (FIQ), a self-administered questionnaire with 10 subscales, measuring fibromyalgia symptoms and function domains (20); the Multidimensional Assessment of Fatigue (MAF), measuring fatigue severity (21); the Pittsburgh Sleep Quality Index (PSQI) measuring sleep quality (22); the Beck II Depression Inventory (BDI) measuring the severity of depressive symptoms (23); the Perceived Stress Scale (PSS) for measuring the perception of stress and current levels of experienced stress (24); and the fibromyalgia tender point count (TPC), examined at each outcome assessment visit (25). For the FIQ, MAF, PSQI, BDI, PSS, and TPC, higher scores indicated a greater perceived severity of the assessed symptom(s); Another of the secondary measures included the Short Form-36 Health Status Questionnaire (SF-36), which measured health-related quality of life (range, 0 to 100, with higher scores indicating better perceived health status) (26). The outcome measures were assessed at baseline and at the end of 4^{th}, 8^{th} and 12^{th} weeks. At the end of the 12-week study, the participants were all self-assessed using the Patient Global Impression of Change (PGIC) questionnaire, to document any perceived change in overall symptom status from the beginning of the study to its conclusion (score range, 1 (very much improved) to 7 (very much worse)) (27).

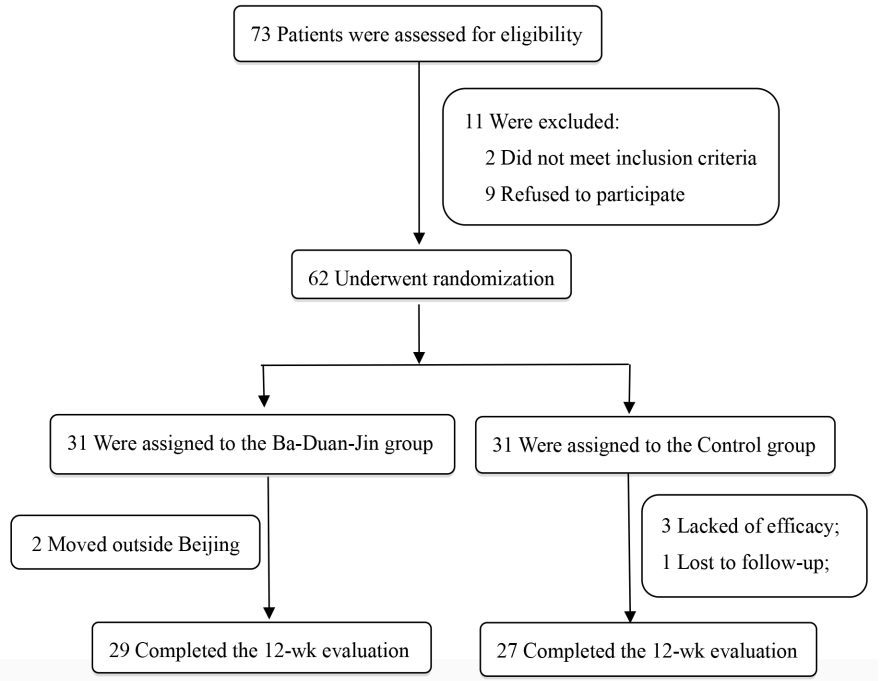

Fig. 1. Screening, assignment and completion of the trial-group.

For the participants in the Ba-Duan-Jin group, there was one additional follow-up interview at week 24, regardless of whether or not they continued the Ba-Duan-Jin exercise at home.

Compliance

Participants were asked not to take part in any other new or additional exercise programmes during the course of the study. If a participant missed a supervised Ba-Duan-Jin practice session, a make-up session was provided.

Concomitant therapy

Participants in both groups were encouraged to continue, for the duration of the study, any pharmacotherapy that had been taken in a stable manner for at least one month. Allowed were non-steroidal anti-inflammatory drugs, acetaminophen (≤1.5 g/day), analgesics, antidepressants, and traditional Chinese medicines. The study subjects were also allowed to continue their regular visits with their physicians throughout the study. The research staff recorded any changes in concomitant therapy, but made no recommendations regarding such changes.

Sample size estimation

A previous Tai Chi trial conducted in the US included 66 participants who were randomly assigned to a Tai Chi group or a control group (11). That study achieved a significant between-group difference in mean pain VAS of -1.9 (95% CI, -1.3 to -0.7), p=0.002. Guided by those findings, it was mathematically-determined that, using a two-sided t-test, a total of 62 fibromyalgia syndrome patients randomised to one of two study groups should provide an 80% power to detect a by-group mean difference between changes in pain VAS at a significance level of 5%

Statistical analysis

Statistical analyses were conducted by a statistician using the intent-to-treat population. All analyses were performed using SAS 8.2 software. The mean, standard deviation, and 95% confidence interval (CI), as well as the number and the percentage, were reported, as appropriate, for continuous variables and categorical variables. The demographic characteristics of the Ba-Duan-Jin and control groups were compared by 2-sample t-test or Mann-Whitney U-test. The standardised mean difference effect size statistical was used for primary and secondary outcomes. Any p-value less than 0.05 was considered to be statistically significant.

Results

All patients were recruited between March of 2015 and May of 2017, according to the protocol approved by the Ethics Committee. Among 73 patients screened (Fig. 1), 71 were newly diagnosed with fibromyalgia onsite, based on the 1990 ACR Research Classification Criteria. Only 2 (2.8%) of the recruited subjects had been previously diagnosed with fibromyalgia. Nine eligible patients declined to participate in the study. The remaining 62 eligible patients were enrolled and randomised into either the Ba-Duan-Jin group or the usual therapy control group.

The rate of patient retention during the 12-week study was 93.5% in the Ba-Duan-Jin group and 87.1% in the control group. Six patients were lost from the study before week 12 for various reasons (Fig. 1).

Table I shows the baseline demographics and clinical characteristics of the two study groups. All of the participants were ethnically Chinese. The mean age of the participants was 51.2 years and 88% were women. The mean body-mass index (BMI) was 23.5, and the mean duration of fibromyalgia-like symptoms was 32.1 months. The mean score on the FIQ, and the physical and the two components of the SF-36 were 46.3, 33.2 and 51.8, respectively. There were no significant by-group differences at baseline in demographics or symptomatic variables between the two study groups.

Primary outcome

The changes in the primary outcome variable, pain VAS, from baseline to week -4, -8, and -12 weeks are shown in Table II and in Figure 2A. By week 4, the Ba-Duan-Jin group had exhibited a significant decrease in the pain VAS score when compared with the control group, -14.7 (95% CI, -21.1 to -8.3) *vs*. -2.4 (95% CI, -6.7 to 1.9), p=0.002. There was a progressive by-group difference in the pain VAS scores favouring the Ba-Duan-Jin group, -21.9 (95% CI, -29.6 to -14.2) at week 8, and -30.8 (95% CI, -38.8 to -22.8) at week 12, compared with those in the control group, -5.5 (95% CI, -11.8 to 0.8), p=0.002, and -4.7 (95% CI, -9.7 to 0.3),

Table I. Demographics and baseline clinical characteristics*.

Characteristic	Ba-Duan-Jin group (n=31)	Control group (n=31)
Age - yr	48.9 ± 10.2	53.5 ± 10.6
Female sex - no. (%)	26 (84)	27 (87)
Disease Duration - months	31.2 ± 43.1	36.5 ± 26.9
Body-mass index†	23.4 ± 2.4	23.6 ± 3.3
Current tobacco use - no. (%)	1 (3)	1 (3)
Current alcohol use - no. (%)	1 (3)	1 (3)
Married status - no. (%)	23 (74)	25 (81)
Education level - no. (%)		
<9 grade	3 (10)	3 (10)
High school	8 (26)	7 (23)
College	17 (55)	19 (61)
Postgraduate	3 (10)	2 (6)
Employment - no. (%)		
Employed	12 (39)	11 (35)
Retired	17 (55)	19 (61)
Unemployed	2 (6)	1 (3)
Previous FM treatment history - no.(%)	13 (42)	15 (48)
Pre-study medications - no.(%)		
Pregabalin	1 (3)	1 (3)
Duloxetine	0 (0)	1 (3)
Amitriptyline	1 (3)	0 (0)
Venlafaxine	2 (6)	0 (0)
NSAIDs	4 (13)	2 (6)
Sedatives	2 (6)	4 (13)
Acupuncture & moxibustion	3 (10)	1 (3)
Chinese medicine	4 (13)	4 (13)
Acupotome ‡	0 (0)	2 (6)
Medicinal paste	2 (6)	1 (3)
Self-reported coexisting illness - no.(%)		
Cardiovascular diseases	5 (16)	8 (26)
Osteoarthrosis/osteoporosis	3 (10)	4 (13)
Tumour	2 (7)	4 (13)
Ovarian cyst/adenomyosis	1 (3)	4 (13)
Respiratory diseases	3 (10)	0 (0)
Depression	2 (7)	1 (3)
Migraine	2 (7)	0 (0)
Irritable bowel syndrome	1 (3)	1 (3)
Temporomandibular arthritis	1 (3)	0 (0)
Pain VAS score §	55.6 ± 20.5	55.2 ± 21.1
FIQ score ¶	46.6 ± 15.4	46.1 ± 16.8
MAF score #	34.0 ± 8.5	31.6 ± 5.3
PSQI score **	10.8 ± 4.2	9.7 ± 3.8
BDI score ††	8.5 ± 5.8	8.3 ± 6.0
PSS score ‡‡	24.1 ± 9.1	23.2 ± 9.7
SF-36 score §§		
Physical component score	35.2 ± 18.5	31.2 ± 15.2
Mental component score	52.8 ± 20.0	50.8 ± 19.2
TPC ¶¶	14.7 ± 2.7	14.7 ± 2.7

*Plus-minus values are mean ± SD unless otherwise noted.
†The body-mass index is the weight in kilograms divided by the square of the height in meters.
‡An acupuncture operation using instrument shaped like a needle knife.
§The visual analogue scales (VAS) for pain (Pain VAS) is a self-report measure of perceived body pain. Scores range from 0 to 100 mm, with higher scores indicating greater pain.
¶The Fibromyalgia Impact Questionnaire (FIQ) assesses fibromyalgia symptoms and function domains. Scores range from 0 to 100, with higher scores indicating more severe symptoms.
#The Multidimensional Assessment of Fatigue (MAF) measure fatigue severity scoring from 0 to 50, with higher scores indicate more severe fatigue.
**Scores on the Pittsburgh Sleep Quality Index (PSQI) range from 0 to 21, with higher scores indicating worse sleep quality.
††The Beck II Depression Inventory (BDI) assesses the severity of depressive symptoms. Scores range from 0 to 39, with higher scores indicate a greater degree of depression severity.
‡‡The Perceived Stress Scale (PSS) is for measuring the perception of stress and current levels of experienced stress. Scores range from 0 to 56, with higher scores indicate a greater degree of symptom severity.
§§The Short Form-36 Health Status Questionnaire (SF-36) is a self-report, 36-item questionnaire that assesses the concepts of physical functioning, role limitations due to physical problems, social function, bodily pain, general mental health, role limitations due to emotional problems, vitality, and general health perceptions. Note that both the physical and mental component summaries can be combined. Scores range from 0 to 100, with higher scores indicating better health status.
¶¶The fibromyalgia tender point count (TPC) is a part of the clinical examination for fibromyalgia ranging from 0 to 18, with higher values indicated a lower pain threshold.

$p<0.001$, respectively. In addition, patients in the Ba-Duan-Jin group experienced remarkable reductions in body pain according to the week-12 self-assessment of the primary outcome variable: 24 out of 31 (77%) of Ba-Duan-Jin treated patients perceived a ≥30% reduction in pain, while only 5 of 31 (16%) among the control subjects experienced a similar level of benefit (Fig. 2B). At the same final self-assessment visit, 17 of 31 (55%) of the Ba-Duan-Jin-treated subjects reported at least a 50% reduction of their perceived pain.

Secondary outcomes

Table II, Figures 3 and 4 present the changes observed among the secondary outcome measures (95% CI) from the baseline to each of the main assessment intervals. By week 4, the Ba-Duan-Jin group showed greater improvement in fibromyalgia symptom severity (FIQ, $p=0.046$), fatigue (MAF, $p=0.02$), and sleep quality (PSQI, $p=0.02$) than were seen with the control group. The decrease in the TPC in the Ba-Duan-Jin group was also significantly greater than that in the control group ($p=0.004$). By week 8 and week 12, the relative improvements in the FIQ, MAF, PSQI, and TPC were even more substantial in the Ba-Duan-Jin group ($Ps \leq 0.004$). There was no significant by-group difference in the mental symptoms domains, including depression (BDI) and stress (PSS), at baseline or at week 4 or at week 8. However, by week 12, the Ba-Duan-Jin group had exhibited a significantly greater improvement in depression and stress than did the control group ($Ps \leq 0.004$). The by-group improvement in the quality of life (QOL, both physical and mental component summaries of the SF-36) was significantly greater in Ba-Duan-Jin group by week 8 ($Ps=0.04$), and continued out to week 12 ($Ps \leq 0.008$).

The PGIC only administered at week 12, the final study visit, required patients to compare their current symptoms with their status at baseline, study entry. Three of the five choices offered "much improved", "somewhat improved" and "not improved" were most often chosen by the completing patients in the study. In Ba-Duan-Jin group,

Table II. Changes from baseline in primary and secondary outcomes*.

Outcome	Change from baseline		Between-Group difference		
	Ba-Duan-Jin Group (n=31)	Control group (n=31)	Ba-Duan-Jin Group *vs*. Control Group	*p*-value†	Effect size‡
Pain VAS					
Week 4	-14. (-21.1 to -8.3)	-2.4 (- 6.7 to 1.9)	-12.3 (-20.0 to -4.6)	0.002	-0.73
Week 8	-21.9 (-29.6 to -14.2)	-5.5 (-11.8 to 0.8)	-16.4 (-26.4 to -6.5)	0.002	-0.87
Week 12	-30.8 (-38.8 to -22.8)	-4.7 (- 9.7 to 0.3)	-26.1 (-35.5 to -16.7)	<0.001	-1.24
FIQ					
Week 4	-9.5 (-14.2 to -4.8)	-3.2 (-6.7 to 0.4)	-6.3 (-12.3 to -0.4)	0.046	-0.63
Week 8	-16.4 (-22.4 to -10.3)	-3.5 (-7.7 to 0.6)	-12.9 (-20.1 to -5.5)	0.002	-0.86
Week 12	-21.4 (-27.2 to -15.5)	-3.5 (-7.7 to 0.8)	-17.9 (-25.1 to -10.7)	<0.001	-1.57
MAF					
Week 4	-5.1 (-8.2 to -1.9)	0.6 (-2.0 to 3.2)	-5.7 (-9.7 to -1.6)	0.02	-0.45
Week 8	-9.4 (-12.8 to -6.1)	-2.0 (-5.4 to 1.4)	-7.4 (-12.2 to -2.7)	0.003	-0.81
Week 12	-12.3 (-15.9 to -8.7)	-3.5 (-6.7 to -0.2)	-8.8 (-13.7 to -4.0)	<0.001	-1.08
PSQI					
Week 4	-1.7 (-2.8 to -0.7)	0.3 (-0.6 to 1.1)	-2.0 (-3.3 to -0.6)	0.02	-0.45
Week 8	-2.6 (-3.8 to -1.4)	-0.0 (-0.8 to 0.8)	-2.6 (-4.0 to -1.2)	0.002	-0.70
Week 12	-3.4 (-4.6 to -2.1)	-0.1 (-0.9 to 0.7)	-3.3 (-4.7 to -1.7)	<0.001	-0.86
TPC					
Week 4	-2.2 (-3.3 to -1.1)	0.1 (-0.8 to 0.9)	-2.3 (-3.6 to -0.9)	0.004	-0.62
Week 8	-3.6 (-4.7 to -2.4)	-0.1 (-0.8 to 0.7)	-3.5 (-4.9 to -2.2)	<0.001	-1.00
Week 12	-6.5 (-7.9 to -5.1)	0.2 (-0.6 to 0.9)	-6.7 (-8.3 to -5.1)	<0.001	-1.56
BDI					
Week 4	-1.0 (-2.6 to 0.6)	-0.3 (-1.7 to 1.1)	-0.7 (-2.8 to 1.5)	0.17	-0.19
Week 8	-3.2 (-5.3 to -1.1)	-1.1 (-2.4 to 0.3)	-2.1 (-4.6 to 0.4)	0.15	-0.48
Week 12	-4.3 (-6.6 to -2.0)	-1.1 (-2.4 to 0.3)	-3.2 (-5.9 to -0.6)	0.004	-0.61
PSS					
Week 4	-0.9 (-2.8 to 1.0)	1.3 (-0.6 to 3.2)	-2.2 (-4.9 to 0.5)	0.12	-0.14
Week 8	-3.0 (-5.5 to -0.5)	0.5 (-1.7 to 2.7)	-3.5 (-6.8 to -0.1)	0.06	-0.34
Week 12	-5.3 (-8.0 to -2.6)	0.5 (-1.5 to 2.5)	-5.8 (-9.1 to -2.4)	0.003	-0.61
SF-36 Physical component score					
Week 4	11.6 (5.8 to 17.4)	6.1 (0.1 to 12.1)	5.5 (-2.8 to 13.9)	0.06	0.57
Week 8	18.1 (10.2 to 25.9)	6.5 (1.9 to 11.0)	11.6 (2.5 to 20.6)	0.04	0.75
Week 12	25.2 (18.6 to 31.8)	8.2 (3.5 to12.9)	17.0 (8.8 to 25.1)	<0.001	1.20
SF-36 Mental component score					
Week 4	6.3 (0.0 to 2.4)	1.1 (-6.2 to 8.3)	5.2 (-4.4 to 14.7)	0.09	0.28
Week 8	13.2 (5.5 to 20.9)	1.5 (-4.4 to 7.4)	11.7 (2.0 to 21.4)	0.04	0.54
Week 12	17.6 (10.8 to 24.4)	3.5 (-2.4 to 9.3)	14.1 (5.1 to 23.1)	0.008	0.78

*All values are means (95% confidence intervals). This table summarises data from patients in the intent-to-treat population who received at least one week of the Ba-Duan-Jin treatment or control monitoring. For Pain VAS, FIQ (both with scores ranging from 0 to 100), MAF (with scores ranging from 0 to 50), PSQI (with scores ranging from 0 to 21), TPC (with scores ranging from 1 to 18), BDI (with scores ranging from 0 to 39), and PSS (with scores ranging from 0 to 56), a higher negative mean change score corresponds to greater decline from baseline among the Ba-Duan-Jin group while a positive treatment difference would favour the control. For the SF-36 PCS and MCS measures (with scores ranging from 0 to 100), the reverse applies. A higher positive mean change score for those SF-36 components corresponds to greater decline from baseline among the Ba-Duan-Jin treatment group while a smaller or even a negative treatment difference would favour the control.

†*p*-values were calculated using the Mann-Whitney U-test, by comparing the changes (95% CI) from the baseline between the Ba-Duan-Jin group and the control group.

‡The standardised mean difference effect size was used for the Ba-Duan-Jin exercise intervention with regard to the primary and secondary outcomes.

there were 18, 9, and 2 of the 29 treated patients who chose "much improved", "somewhat improved", and "not improved"; while there were 2, 10, and 15 of 27 patients in the control group who chose those responses, respectively. The by-group statistical comparisons of the study subjects' responses to these choices highly favoured Ba-Duan-Jin therapy ($p<0.001$).

Concomitant therapy

Nearly half (42%) patients in Ba-Duan-Jin group and 48% in the control group had previously received symptomatic treatment with pregabalin, duloxetine, amitriptyline, estazolam, or traditional Chinese medicines for variable durations. At the time of enrolment, only 9.7% in the Ba-Duan-Jin group and 12.9% in the control group were taking medications, including acetaminophen, loxoprofen sodium, venlafaxine, and traditional Chinese medicines. As instructed, that minority of patients continued to take their pre-study medications for the duration study.

Adverse event

There was one participant who reported experiencing mild knee pain after three

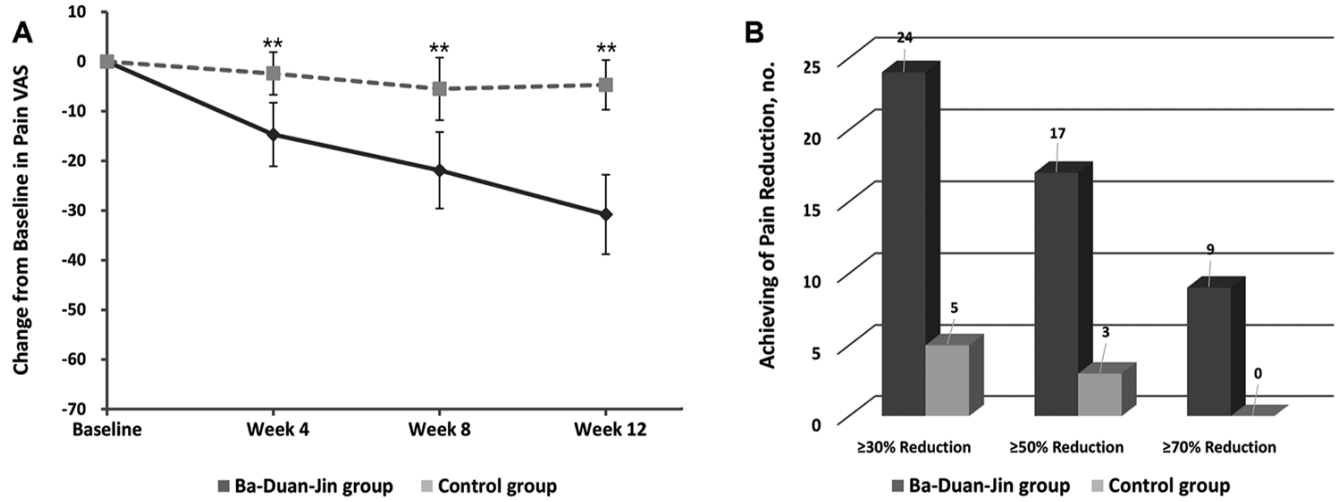

Fig. 2. A. Mean changes from baseline in pain VAS. **B.** The number of patients achieving pain reduction at week 12.
Figure A on the left shows the outcome scores for the Ba-Duan-Jin group (diamonds) and the control group (squares). Measurements are the changes obtained at weeks 4, 8, and 12. I bars indicate 95% CI; single asterisk (*) indicates *p*-values <0.05 by comparing the changes (95% CI) from the baseline between the Ba-Duan-Jin group and the control group; double asterisks (**) indicate *p*-values <0.01 by comparing between the 2 groups. Scores on the Multidimensional Assessment of Fatigue (MAF) range from 0 to 50, with higher scores indicating more severe fatigue. Pittsburgh Sleep Quality Index (PSQI) range from 0 to 21, with higher scores indicating worse sleep quality. Tender Points Count (TPC) range from 0 to 18, with higher scores indicating more TPC. Negative changes from baseline indicated improvement on the FIQ, MAF, PSQI and TPC, with lower scores indicating improvement.
Figure B on the right shows the number of patients achieving pain reduction ≥30%, ≥50%, ≥70% at week 12 for the Ba-Duan-Jin group (black) and the control group (grey). Higher number indicated more achievement.

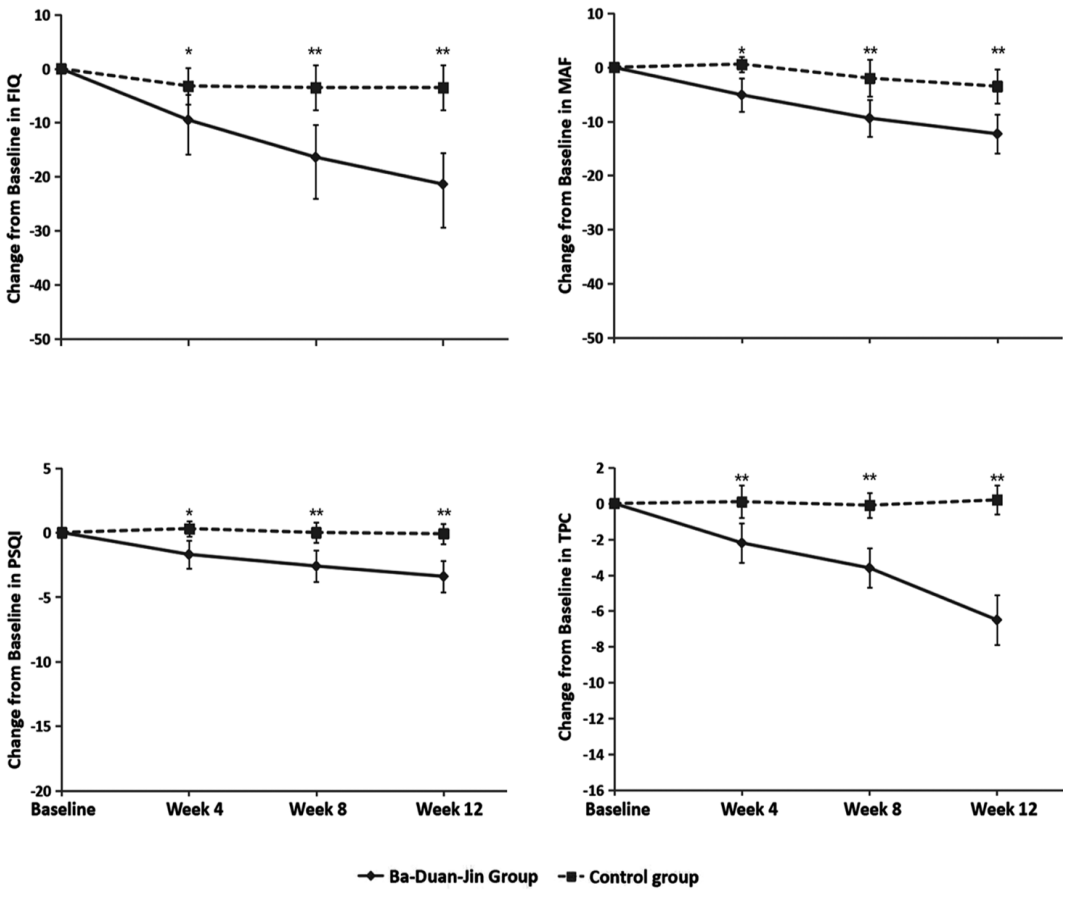

Fig. 3. Mean changes from baseline in secondary outcomes: physical improvement. Outcome scores are shown for the Ba-Duan-Jin group (diamonds) and the control group (squares). Measurements are the changes obtained at week 4, 8, and 12. I bars indicate 95% CI; single asterisk (*) indicates *p*-values <0.05 by comparing the changes (95% CI) from the baseline between the Ba-Duan-Jin group and the control group; double asterisks (**) indicate *p*-values <0.01 by comparing between the 2 groups. Scores on the Multidimensional Assessment of Fatigue (MAF) range from 0 to 50, with higher scores indicating more severe fatigue. Pittsburgh Sleep Quality Index (PSQI) range from 0 to 21, with higher scores indicating worse sleep quality. Tender Point Count (TPC) range from 0 to 18, with higher scores indicating more symptomatic tender points. Negative changes from baseline indicate improvement on the FIQ, MAF, PSQI and TPC, with lower scores indicating improvement.

weeks of Ba-Duan-Jin practice. That symptom was attributed to the patient's incorrect posture during the exercises; after a 2-week rest and correction of the posture problem, that patient resumed the practice of Ba-Duan-Jin and completed the study without other sequele. No other adverse effects were reported from either of the two study groups.

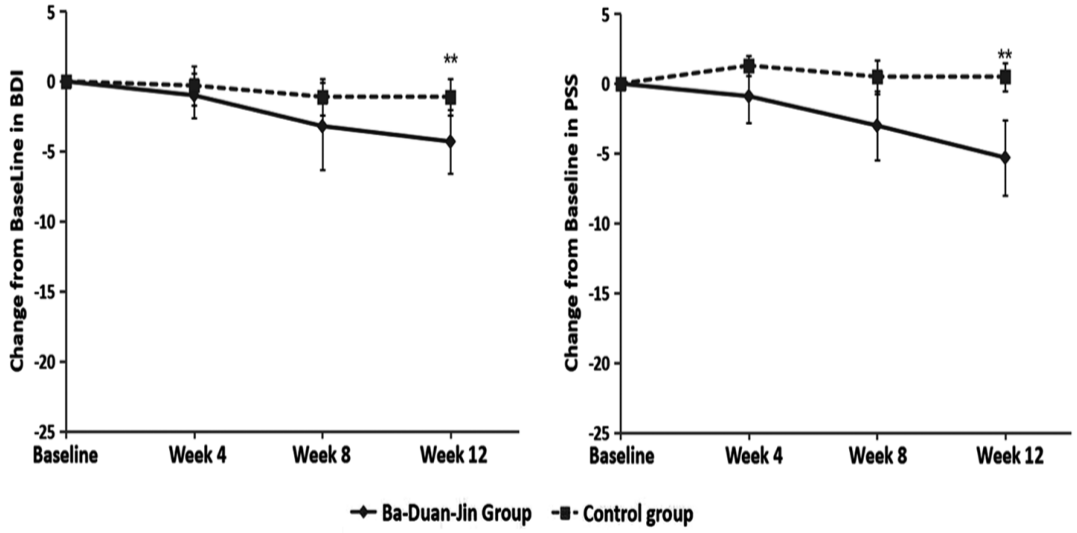

Fig. 4. Mean changes from baseline in secondary outcomes: mental improvement.
Outcome scores are shown for the Ba-Duan-Jin group (diamonds) and the control group (squares). Measurements are the changes obtained at week 4, 8, and 12. I bars indicate 95% CI; double asterisks (**) indicate *p*-values <0.01 by comparing the 2 study groups. The Beck Depression Inventory (BDI) provides scores ranging from 0 to 39, wherein higher scores indicated more severe depression, while the Perceived Stress Scale (PSS) provides scores ranging from 0 to 56, with higher scores indicating a perception of higher stress levels. With both instruments negative changes from baseline indicate improvement since lower scores indicate improvement in both of these affective manifestations.

Discussion

In this randomised, usual-therapy-controlled study, it was found that supervised Ba-Duan-Jin exercise twice weekly for 12 weeks by Chinese fibromyalgia patients resulted in significant reductions of pain, fatigue, sleep disturbance, affective symptoms, and symptomatic tender-points. The same patients perceived to have improved their physical function and global health status. The results support Ba-Duan-Jin exercise as a beneficial therapy for Chinese patients with fibromyalgia. Adverse effects were minimal and suggest that Ba-Duan-Jin is safe therapy for such patients. A reasonable question is whether Ba-Duan-Jin therapy can achieve similar benefits for fibromyalgia syndrome patients of other ethnic backgrounds and other forms of cultural heritage.

The best answer to that question is "probably yes". Other forms of Qigong exercise such as Tai Chi, have been useful for fibromyalgia patient management in Western clinical studies (11, 28, 29). In addition, the current findings that Ba-Duan-Jin can help patients with fibromyalgia are consistent with its known beneficial effects in other chronic medical conditions (13-17). The outcome domains of pain, physical function, sleep or fatigue, and the additional domains of depression, anxiety or cognition has been formed into a responder set to identify the response to pharmacological treatment among patients with fibromyalgia (30). Currently, there has been some effort to develop responder criteria for research regarding non-pharmacological interventions (31). It certainly would be of interest to utilise the proposed responder criteria in the interpretation of future studies of non-pharmacological interventions when those responder criteria have been well formulated and experimentally validated.

The Chinese patients in this study were found to be demographically similar to the fibromyalgia patients characterised in previously published Western Qigong clinical trials (11, 28, 29) with respect to age, gender and educational level, but differ in a few other aspects. At baseline, the Chinese cohort had a shorter duration of fibromyalgia-related complaints (<3 years), normal BMI, an average pain VAS of 55/100, and fibromyalgia-related symptoms severity score FIQ at 46. By contrast, the fibromyalgia patients in Western studies had a longer duration of symptoms (average 10 to 18 years), were overweight or obese, had more severe pain (pain VAS >60/100), and had higher FIQ scores (>60 points) (11, 28, 29). There is no data to indicate whether Ba-Duan-Jin would offer the same magnitude of benefit for patients with a longer duration of fibromyalgia, higher BMI, and more severe pain. Since culture can influence self-reporting of pain severity, it is not possible to conclude that the average pain severity was actually greater in the Western study fibromyalgia patients.

It is notable that significant improvement of the core fibromyalgia symptoms including pain (pain VAS), fatigue (MAF), sleep (PSQI), tender points (TPC), and the impact of fibromyalgia (FIQ) appeared only 4 weeks of Ba-Duan-Jin exercise and continued to a expand with continuation of the practice. Notice also that improvements in the Chinese patients' perception of QOL (both SF-36 physical and mental components) continued out to 8 and 12 weeks. In contrast, the psychological domains including depression and stress did not exhibit significant improvement until week 12. One possibility is that Qigong practice leads to changes in physical state, such as blood circulation, respiration, certain nervous pathways, and/or levels of inflammation, more rapidly than does the psychological state. The emotive manifestations might require a longer duration of treatment to modulate, akin to how

it takes psychoactive medications 4-8 week to become effective. An area for further research could involve collecting biological samples to try to understand the mechanisms responsible for these changes.

The authors acknowledge several limitations to this study: 1) the lack of awareness of fibromyalgia in mainland China made it necessary for the investigators to inform and educate the participants regarding their condition in a relative vacuum of general knowledge about this condition; 2) the participants were recruited from the outpatient rheumatology clinic of a tertiary medical centre for the Beijing region of China, which may have resulted in selection bias toward more severely-affected patients with more psychologic overlay. It is clear that multicentre randomised controlled clinical trials with larger sample sizes of fibromyalgia patients are needed to ascertain which patients may benefit most from Ba-Duan-Jin; 3) the study was designed to have the control group continue their usual therapy for a full 12 weeks, and then be offered the option to begin practicing supervised Ba-Duan-Jin exercise for a subsequent 12 weeks. A good fortune of this study was that the control group remained compliant with the requirements of the study design. Clearly, a large exodus of control group subjects would have represented a serious limitation for this study; 4) other pain conditions commonly overlap with fibromyalgia syndrome, and treatment of comorbid conditions probably has an impact on the management of fibromyalgia pain (32). There were several patients with apparently independent comorbid diseases (23% in Ba-Duan-Jin group, 19% in control group), including ovarian cyst/adenomyosis, depression, migraine, irritable bowel syndrome and temporomandibular arthritis, which were self-reported to be stable when the patients enrolled in the study.

The forms used to assess the characteristic manifestations of fibromyalgia had to be idiomatically translated from their original languages into Chinese. Some of those instruments had already been validated in their Chinese-language forms (BDI, PSQI, PSS, SF-36) but validations of others are still pending (FIQ, MAF, PGIC). Both of the conditions in the 1990 ACR diagnostic criteria for fibromyalgia are objective and the 1990 ACR Research Classification Criteria have provided a basis for subsequent criteria. There is still no validated Chinese language version of the 2011 ACR criteria instrument form for the diagnosis of fibromyalgia. Therefore, this study was dependent upon the 1990 ACR Research Classification Criteria as a validated approach to identification of fibromyalgia patients for the purpose of clinical research. Our research group has begun the necessary regional tasks of idiomatic translation and validation of many fibromyalgia diagnostic and outcome assessment instruments (ClinicalTrials.gov identifier: NCT03381131).

Due to the current general lack of awareness of fibromyalgia among the Chinese general public, and even among health care providers in China, a group of Chinese investigators has been organised to disseminate information and further study fibromyalgia in China, including the therapeutic potential for Ba-Duan-Jin therapy in fibromyalgia patients. Efforts are already underway to determine the epidemiology and natural history of the fibromyalgia in China. An earlier epidemiology study conducted in Hong Kong reported a 1% prevalence of fibromyalgia in that region (33) but it is unclear whether the same will be true for mainland China. If the fibromyalgia is equally prevalent in mainland China, it would be reasonable to estimate that over 14 million persons in China have fibromyalgia. In addition, there are already plans in China to study the effects of established pharmacotherapy in combination with Ba-Duan-Jin as the non-pharmacotherapy intervention. In the current study, physician investigators served as the instructors and exercise session leaders. However, training non-physician personnel to implement such a program would improve practicality, reduce costs, and encourage wider use of these techniques for fibromyalgia patients.

In summary, Ba-Duan-Jin appears to be a safe and an effective therapy for Chinese patients with the fibromyalgia syndrome. Fortunately, Ba-Duan-Jin was readily accepted by Chinese fibromyalgia patients, perhaps because of their long cultural heritage of treatment with such interventions. It is unknown how well Ba-Duan-Jin would be accepted by fibromyalgia syndrome patients and their caregivers from other countries and cultures. Although the mechanism responsible for the benefit of Ba-Duan-Jin in fibromyalgia is still unclear, it certainly seems to be inexpensive. Thus, it has the potential to be a valuable non-pharmacological addition to the world-wide therapeutic armamentarium of physicians caring for fibromyalgia syndrome patients.

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