ORIGINAL RESEARCH

Exercise Plus Acupuncture on Consensus Acupoints Versus Acupoints Selected by the Theory of Equal Impact on Tendons, Bones, and Muscles for Knee Osteoarthritis

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ABSTRACT

Context • Knee osteoarthritis (KOA) is a degenerative disorder that significantly affects patients' quality of life. Acupuncture and exercise are the most popular treatments currently. The outcomes for acupuncture for KOA, however, are controversial, with some researchers finding that the addition of acupuncture to exercise therapy provided no additional improvement in pain scores.

Objective • The study intended to evaluate the therapeutic effects for KOA of exercise in combination with acupuncture on acupoints selected using the Traditional Chinse Medicine (TCM) theory of Equal Impact on Tendons, Bones, and Muscles (EITBM) in comparison with that of acupoints selected using classical consensus for the treatment.

Design • The research team performed a randomized controlled trial.

Setting • The study took place in the Department of Acupuncture and Moxibustion at the First Affiliated Hospital of Hebei University of Chinese Medicine in Shijiazhuang, Hebei, China.

Participants • Participants were 70 patients with KOA who visited the hospital between December 2020 and February 2021.

Intervention • Participants in both group received acupuncture plus exercise therapy. The research team randomly assigned participants to one of two groups: (1) 35 to the intervention group, which received acupuncture using acupoints selected using EITBM, and (2) 35 to the control group, which received acupuncture using the classical consensus acupoints. Both groups performed a 25-min session of acupuncture three times weekly for 4 weeks, with the exercise therapy following the acupuncture each time.

Outcome Measures • The research team assessed clinical efficacy at baseline and postintervention. The primary outcome measures included assessments: (1) of knee joint pain using a visual analog scale (VAS), (2) of knee joint pain, flexibility, and function using the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) pain subscale; and (3) joint range of motion (ROM). The secondary outcome measures included measurement of serum levels of interleukin-1 beta (IL-1ß), tumor necrosis factor alpha (TNF-α), and matrix metalloproteinase-13 (MMP-13) using enzyme-linked immunosorbent assays (ELISA).

Results • The VAS and WOMAC scores significantly decreased for both groups between baseline and postintervention, and the intervention group's decrease was significantly greater than that of the control group. The ROM of knee flexion was significantly higher in both groups postintervention than at baseline, and the intervention group's increase was significantly higher than that of the control group. The serum IL-1ß, TNF-α, and MMP-13 also significantly decreased postintervention in both groups, and the intervention group's levels were significantly lower than those of the control group. The total effective rate was 94.1% in the intervention group, 32 out of 34 participants, and 75.8% in the control group, 25 out of 33 participants, which was significantly different.

Conclusions • Acupuncture, in combination with exercise, can relieve symptoms, improve joint function, and reduce pro-inflammatory cytokines (IL-1ß and TNF-a) as well as MMP-13 for patients with KOA. The outcomes for acupuncture using EITBM acupoints were significantly better than those of the acupoints selected using classical consensus. (*Altern Ther Health Med.* 2023;29(5):262-267).

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Knee osteoarthritis (KOA) is a degenerative disorder that significantly affects patients' quality of life (QoL). The incidence of osteoarthritis in the Chinese population is approximately 10% of the general population, and over 50-million patients currently suffer from KOA in China.[1] In the USA, the prevalence of KOA was 16% of the general population in the late twentieth century, and that rate has doubled since the mid-twentieth century.[2]

The American College of Rheumatology (ACR) published guidelines for the treatment of KOA in 1995[3] and updated them in 2000.[4] The European League Against Rheumatism also published guidelines for KOA treatment in 2000.[5] Those guidelines address nonpharmacological and pharmacological management of the symptoms of KOA patients.

For that management, clinicians suggest nonpharmacological therapies, which include patient education, physical therapy, occupational therapy, and exercise, as the first line of treatment. The 2000 update of the ACR guidelines[4] mentions acupuncture as a therapeutic approach under investigation. Acupuncture and exercise are the most popular treatments currently.

Acupuncture

For pain relief, clinicians often treat patients with KOA with nonpharmacological options or complementary medicine,[13] and practitioners have clearly used acupuncture as a nonpharmacological treatment for KOA in China as well as in Europe and America.

The outcomes for acupuncture for KOA, however, are controversial. A study with 352 adults aged 50 or older with a clinical diagnosis of KOA, at 37 physiotherapy centers in the UK, found that the addition of acupuncture to a course of exercise for KOA provided no additional improvement in pain scores.[14]

A systemic review and meta-analysis of 13 randomized, controlled clinical trials, however, demonstrated that acupuncture that meets the criteria for adequate treatment was significantly superior, both to sham acupuncture and to no additional intervention, for improving pain and function in patients with chronic knee pain.[15]

Two studies, however, found that acupuncture can improve KOA symptoms and function clinically.[6,7] The more recent of those studies, a randomized controlled trial of 480 patients with KOA in China demonstrated that intensive electroacupuncture resulted in less pain and better function at week 8 compared with sham acupuncture, and the effects persisted through week 26.[7]

Exercise Therapy

Clinicians consider exercise therapy to be one of the key methods for management of KOA. Initiating knee-joint actions and alleviating loading requires normal quadricep-muscle strength.[31,32] Impairments of the muscles of KOA patients, however, can cause some exercise, such as quadricep sets, to puts patients at high risk of pain and functional limitations.[32-34]

Although long-term adherence to exercise therapy remains a challenge for patients,[35] limiting its efficacy, exercise therapy for the musculature is one of the most popular methods for management of KOA in clinical practice, and studies have confirmed that exercise can be conducive to restoring an imbalance of musculature and that it can prevent or treat muscle impairments in KOA patients.[32,34,36]

Traditional Chinese Medicine (TCM)

Traditional Chinese Medicine considers KOA to be a deficit of liver, spleen, and kidney functions and an imbalance of tendons, bones, and muscles surrounding the knee joints, which are the sites where KOA originates. Thus, TCM's principle of KOA treatment is not only to treat symptoms, including pain and stiffness of the joint, but also to treat the cause of the KOA, which requires restoring the balance and function of tendons, bones, and muscles around the joints.

TCM treatments can effectively relieve KOA symptoms with acupuncture because it can tonify Qi and blood by stimulating and smoothing meridians, which promotes the release of central analgesic transmitters, such as opioid peptides.[30]

Pathogenesis of KOA

While the pathogenesis of KOA remains to be defined, studies in Western medicine have shown that chondrocytes' apoptosis is one of the potential causes of development of KOA.[16] Pro-inflammatory cytokines—interleukin-1 beta (IL-1ß) and tumor necrosis factor alpha (TNF- α)—and matrix metalloproteinases (MMPs), which the transcription factor nuclear factor kappa B (NF-kB) regulates, play an important role in the initiation of apoptosis and matrix degradation.[17-19]

MMP-13 is capable of degrading type II collagen in cartilage,[20,21] and the severity of KOA correlates with the levels of IL-1ß, TNF-a, and MMP-13.[22-24] Furthermore, although the therapeutic mechanisms of acupuncture for KOA aren't well understood, the following mechanisms are very likely involved in acupuncture's ability to alleviate pain and promote functional recovery for KOA patients: (1) suppression of the release of inflammatory cytokines such as IL-1ß, IL-6, and TNF-a; (2) inhibition of signal transduction pathways that are associated with pain and tissue damage[25-27]; and (3) promotion of antioxidant synthesis and release.[28,29]

Current Study

The current study intended to evaluate the therapeutic effects for KOA of exercise in combination with acupuncture on acupoints selected using the TCM theory of the Equal Impact on Tendons, Bones, and Muscles (EITBM) in comparison with that of acupoints selected using classical consensus.

METHODS

Participants

The research team performed a randomized controlled trial. The study took place in the Department of Acupuncture and Moxibustion at the First Affiliated Hospital of Hebei University of Chinese Medicine in Shijiazhuang, Hebei, China. Potential participants were patients with KOA who visited the hospital between December 2020 and February 2021.

The study included potential participants if they: (1) were 40-75 years old; (2) met the diagnostic criteria for KOA following the American College of Rheumatology's (ACR's)

Guidelines for the Medical Management of Osteoarthritis: Part II. Osteoarthritis of the Knee[4]; (3) met the diagnostic criteria for QiPi, the TCM term for KOA, following the guidelines in *Diagnosis and Treatment Criteria of Traditional Chinese Medicine*[8]; (4) had KOA that was grade ≤ III under the Kellgren-Lawrence guidelines; and (5) had never been involved in any clinical trial.

The diagnosis of KOA required potential participants to meet the ACR's guidelines for criteria 1 and 2, plus any one of the remaining criteria: (1) knee joint pain, (2) a radiological examination showing osteophytes, (3) an age of 50 years or older; (4) knee-joint stiffness in the morning that lasts less than 30 min, and (5) fricative sounds in the knee joints.

The diagnosis of QiPi required potential participants to meet the following guidlines[8]: (1) mild knee joint pain and joint stiffness, for which light exercise provides relief but rainy days makes worse; (2) vicious recycling and worsening of those symptoms; (3) mild swelling and fricative sounds at the knee joints; and (4) possibly muscle atrophy and joint deformity.

The study excluded potential participants if they: (1) had had knee-joint surgery; (2) had had a twisted knee joint, torn meniscus, rheumatoid arthritis, tuberculosis, infections, or injury; (3) had a skin rash around the knee joints or an abnormal blood-coagulation function; (4) had had other complications, such as tumors, cardiovascular diseases, active gastric ulcers, or bleeding; or (5) were pregnant or breast feeding, or expecting to undergo fertilization.

Participants signed a written Informed Consent Form and agreed to participate into the study. The Ethics Committee of the Hebei Province Hospital of Traditional Chinese Medicine (HBZY2020-KY-082-01) approved the study's protocols, and the research team registered the study at the Chinese Clinical Trial Registry (No. ChiCTR2100054529).

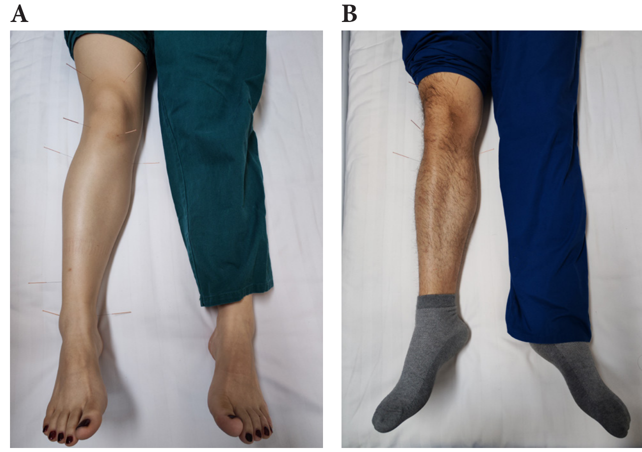
Procedures

Randomization. The research team randomly assigned the participants to the intervention group or the control group, with the participants having even numbers being assigned to the intervention group and those having odd numbers being assigned to control group.

Interventions. Participants in both group received acupuncture plus exercise therapy. The research team performed a 25-min session of acupuncture three times weekly for 4 weeks, with the exercise therapy following the acupuncture each time. The intervention group received acupuncture using acupoints selected using EITBM, and the control group received acupuncture using the classical-consensus acupoints. The research team selected the EITBM acupoints by referring to the National Criteria of Nomenclature and Location of Acupuncture Points.[9]

Outcome measures. The research team assessed clinical efficacy. The primary outcome measures included assessments: (1) of knee joint pain using a visual analog scale (VAS)[10]; (2) of knee joint pain, flexibility, and function using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale[11]; and (3) of range of motion (ROM).

Figure 1. Acupoint Selection and Acupuncture Treatment for Participants With Knee Osteoarthritis. Figure 1A shows the acupoint selection using the theory of Equal Impact on Tendons, Bones, and Muscles, and Figure 1B shows the acupoint selection using classical consensus.



The secondary outcome measures included measurement of serum levels of IL-1ß, TNF-α and MMP-13, using enzyme-linked immunosorbent assays (ELISA) and following the manufacturers' instruction. The research team purchased IL-1ß and TNF-a kits from NeoBioscience (Shenzhen, China, Catalog numbers: EHC002B; EHC103A) and MMP-13 from Shanghai Westang Bio-Tech (Shanghai, China, F01920).

Interventions

Acupuncture, intervention group. The research team performed the acupuncture on nine acupoints (Figure 1A): (1) GB39 (Xuanzhong), (2) BL60 (Kunlun), (3) KI13 (Taixi), (4) ST34 (Liangqiu), (5) SP10 (Xuehai), (6) SP9 (Yinlingquan), (7) GB34 (Yanglingquan), (8) LE (Neiqiyan), and (9) ST35 (Dubi). The team: (1) after disinfection of the acupoints, vertically inserted 0.30 mm x 40 mm needles to the depth of 15-30 mm, depending on the points; (2) manipulated the needles to achieve the *de qi* sensations—soreness, numbness, distention, heaviness, and a warm or tingling sensation; and (3) left the needles for 25 minutes under the form of therapy aiming for tonification. Tonifying the deficit in liver, spleen, and kidney function was the main manipulation during the course of acupuncture.

Acupuncture, control group. The research team performed acupuncture on six acupoints (Figure 1B): (1) ST34 (Liangqiu), (2) SP10 (Xuehai), (3) LE (Neiqiyan), (4) ST35 (Dubi), (5) SP9 (Yinlingquan), and (6) GB34 (Yanglingquan). The methods of acupuncture manipulation were same as for the intervention group.

Exercise therapy, both groups. The exercise therapy included: (1) quadricep isometric contraction exercise, in which participants lay in a supine position, tightening the quadriceps with ankle dorsiflexion and pushing the patella upward for 10 s and relaxing for 10s, repeating the exercise 10 times as one session with two sessions each time; (2) knee flexibility exercise, in which participants actively and slowly did flexion and extension of the knee joints in a supine position, 10 times as one session with two sessions each time; (3) knee extension exercise, in which participants lay in a supine position with lifted heels, 10-15 in high on a pillow, and the therapist gently pressed the patella for 30 s, 3-5 times; (4) knee flexion exercise, in which participants were in a prone position, and the therapist extended participants' muscles of the knee extensor group for 15-30s , by holding participants' hip pelvises with one hand and ankles with the other hand, repeated 3-5 times; and (5) active resistance training, in which participants were in a sitting position and kept their hip joints and knee joints at a 90° position, and the therapist loaded 30% resistance for the first and second exercise for knee extension, 70% resistance for the third and fourth try, and 100% resistance at the fifth try, repeating the exercise 5 times for each session, with two sessions each time.

Outcome Measures

VAS and WOMAC. [10] The VAS scores ranged from 0 to 10, with 10 = the most serious pain. The WOMAC scores ranged from 0 to 96, and the higher the score is, the worse the KOA.

ROM. The research team used the degree of the knee joint after actively bending the knee joint to measure ROM of the knee joint. Participants were in a supine position, and the research team actively bent the knee joint, measuring the knee joint's angle, which ranged 0° to 130°. The larger the angle is, the worse ROM is.

Efficacy. The research team evaluated the therapeutic outcomes using the WOMAC scores, following the *Principal Guideline on the Clinical Research of New Herbs*.[12] The rate of symptom reduction (%) = [(baseline WOMAC score – postintervention WOMAC score) / baseline WOMAC score] x 100%.

The rates included: (1) cured—symptom reduction of ≥ 90% with knee joint pain disappearing and normal knee function; (2) significantly effective— symptom reduction of ≥ 60% but ≤ 89% and significant relief of knee joint pain, with the participant being able to go back to work and daily life with functional knee joints; (3) effective—symptom reduction of ≥ 30% but ≤ 59%, with knee joint pain reduced, motion of knee joints being mildly limited, and ability to participate in daily life and job activity being improved; (4) no effect—symptom reduction ≤ 29%, with no improvement in knee joint pain or function.

Effective rate (%) = [(Number of cured + significantly effective + effective) / total number of KOA in the intervention or control group] x 100%.

Statistical Analysis

The research team analyzed all data using SPSS 26.0 software (IBM, Armonk, NY, USA). The team: (1) expressed measurement data as means ± standard deviations (SDs) and compared paired data in compliance with normal distribution between the two groups using the paired *t* test, and compared data without normal distribution using the nonparametric test, and (2) expressed counting data as frequencies (n) and percentages (%) and compared data using the Chi-square test, χ^2. $P < .05$ was considered to be statistically significant.

RESULTS

Participants

The research team enrolled 70 participants in the study, 35 in each group (Figure 2). The team excluded one participant in the intervention group from data analysis because of poor compliance with the treatment protocol. In the control group, one participant dropped out, and the research team lost contact with one participant.

Table 1 shows the demographic and clinical characteristics of the two groups. The control group included 7 males and 26 females, with a mean age of 51.7 ± 6.0, and the intervention group included 5 males and 29 females, with a mean age of 51.6 ± 6.1. No significant differences existed between the groups in terms of age, gender, course of KOA, or BMI ($P > .05$).

Efficacy Rate

In the control group, the interventions were effective for 25 out of the 33 participants (75.8%). In contrast, in the intervention group, the interventions had therapeutic efficacy for 32 out of 34 patients (94.1%), which was significantly higher than that of control group ($P = .045$).

VAS and WOMAC Scores

Table 3 shows that the VAS and WOMAC scores significantly decreased for both the intervention and the control groups between baseline and

Figure 2. Flow Chart of Participants' Enrollment

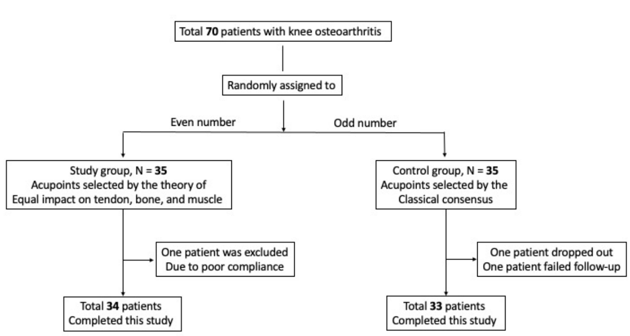


Table 1. Participants' Demographic and Clinical Characteristics (N = 67)

Groups	n	Gender: Male n (%)	Gender: Female n (%)	Age, y Mean ± SD	KOA History, y Mean ± SD	BMI Mean ± SD	KOA: Unilateral n (%)	KOA: Bilateral n (%)
Control	33	7 (21.2)	26 (78.8)	51.7 ± 6.0	5.1 ± 1.9	24.6 ± 4.6	9 (27.3)	24 (72.7)
Intervention	34	5 (14.7)	29 (85.3)	51.6 ± 6.1	5.6 ± 2.9	24.5 ± 6.1	6 (17.6)	28 (82.4)
χ^2/ *t*		0.482		0.068	0.832	0.076	0.893	
P value		.487		.946	.408	.940	.344	

Abbreviations: BMI, body mass index; KOA, knee osteoarthritis.

Table 2. Comparison of Efficacy (N = 67)

Groups	n	Cured n (%)	Significantly Effective n (%)	Effective n (%)	No Effect n (%)	Effective Rate n (%)
Control	33	4 (12.1)	11 (33.4)	10 (30.3)	8 (24.2)	25 (75.8)
Intervention	34	5 (14.7)	14 (41.2)	13 (38.2)	2 (5.9)	32 (94.1)
χ^2						-
P value	0.045[a]					

[a]*P* < .05, indicating that the effective rate was significantly greater in the intervention group than in the group

Table 3. Comparison of the Changes in the VAS and WOMAC Scores of the Intervention and Control Groups Between Baseline and Postintervention and Between Groups (N = 67)

Groups	n	VAS Score Baseline Mean ± SD	VAS Score Postintervention Mean ± SD	*t*	*P* value
Control	33	6.03 ± 1.21	4.37 ± 1.23	15.132	<.001[a]
Intervention	34	6.06 ± 0.95	3.05 ± 1.25	7.220	<.001[a]
t		0.113	4.356		
P value		.910	<.001[#]		
Groups	**n**	**WOMAC Score Baseline Mean ± SD**	**WOMAC Score Postintervention Mean ± SD**	***t***	***P* value**
Control	33	70.73 ± 13.69	32.06 ±12.17	13.082	<.001[a]
Intervention	34	69.53 ± 10.71	28.17 ± 10.34	19.784	<.001[a]
t		0.400	1.412		
P value		.690	**.033**[b]		

[a]*P* < .05, indicating that the decreases in the VAS and WOMAC scores between baseline and postintervention were significant for both groups
[b]*P* < .05, indicating that the VAS and WOMAC scores were significantly lower postintervention in the intervention group than in the control group

Abbreviations: VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

postintervention with all *P* < .001. More important, the intervention group's scores postintervention, at 3.05 ± 1.25 for the VAS and 28.17 ± 10.34 for the WOMAC, were significantly lower than those of the control group, at 4.37 ± 1.23 for the VAS and 32.06 ± 12.17 for the WOMAC, with *P* < .001 and *P* = .033, respectively.

ROM

Consistent with the improvement in symptoms, both groups' knee function also significantly improved (Table 4). The control group's ROM at baseline was 110.76 ± 4.41 and postintervention was 114.03 ± 5.63 (*P* = .001). The intervention group's ROM at baseline was 109.82 ± 3.49 and postintervention was 119.29 ± 6.32 (*P* < .001). Moreover, postintervention, the intervention group's ROM was significantly greater than that of the control group (*P* < .001).

Table 4. Comparison of the Changes in the ROM of the Intervention and Control Groups Between Baseline and Postintervention and Between Groups (N = 67)

Groups	n	ROM Baseline Mean ± SD	ROM Postintervention Mean ± SD	*t*	*P* value
Control	33	110.76 ± 4.41	114.03 ± 5.63	3.487	.001[a]
Intervention	34	109.82 ± 3.49	119.29 ± 6.32	7.863	<.001[a]
t		0.969	3.593		
P value		.336	<.001[b]		

[a]*P* < .05, indicating that the increases in the ROM between baseline and postintervention were significant for both groups
[b]*P* < .05, indicating that the ROM was significantly greater postintervention in the intervention group than in the control group

Abbreviations: ROM, range of motion.

Table 5. Comparison of the Changes in Serum IL-1ß, TNF-a, and MMP-13 of the Intervention and Control Groups Between Baseline and Postintervention and Between Groups (N = 67)

Groups	n	IL-1ß Baseline pg/mL Mean ± SD	IL-1ß Postintervention pg/mL Mean ± SD	*t*	*P* value
Control	33	21.2 ± 0.5	18.7 ± 0.4	22.634	<.001[a]
Intervention	34	20.9 ± 1.7	16.8 ± 1.5	10.545	<.001[a]
t		0.974	7.131		
P value		.334	<.001[b]		
Groups	**n**	**TNF-a Baseline pg/mL Mean ± SD**	**TNF-a Postintervention pg/mL Mean ± SD**	***t***	***P* value**
Control	33	21.9 ± 0.5	17.6 ± 0.7	28.715	<.001[a]
Intervention	34	21.1 ± 0.8	14.8 ± 0.7	34.557	<.001[a]
t		4.891	16.369		
P value		**<.001**	<.001[b]		
Groups	**n**	**MMP-13 Baseline pg/mL Mean ± SD**	**MMP-13 Postintervention pg/mL Mean ± SD**	***t***	***P* value**
Control	33	22.5 ± 4.2	19.4 ± 0.4	4.221	<.001[a]
Intervention	34	21.7 ± 2.1	16.4 ± 3.3	7.901	<.001[a]
t		0.991	5.184		
P value		.326	<.001[b]		

[a]*P* < .05, indicating that the decreases in serum IL-1ß, TNF-a, and MMP-13 between baseline and postintervention were significant for both groups
[b]*P* < .05, indicating that serum IL-1ß, TNF-a, and MMP-13 were significantly lower postintervention in the intervention group than in the control group

Abbreviations: IL-1ß, interleukin-1 beta; TNF-a, tumor necrosis factor alpha; MMP-13, matrix metalloproteinase-13.

Pro-inflammatory Cytokines

Table 5 shows that the levels of IL-1ß, TNF-a, and MMP-13 had significantly decreased from baseline to postintervention, both for the intervention group, with all $P<.001$, and for the control group, with all $P<.001$. Furthermore, postintervention, the intervention group's reductions in IL-1ß to 16.8 ± 1.5, in TNF-a to 14.8 ± 0.7, and in MMP-13 to 16.4 ± 3.3, were significantly greater than those of the control group, at IL-1ß to 18.7 ± 0.4, at TNF-a to 17.6 ± 0.7 ($P<.05$), and MMP-13 to 19.4 ± 0.4, with all $P<.001$,

DISCUSSION

Consistent with the findings of Tu et al's study,[7] the current study demonstrated that patients with KOA can achieve a reduction in VAS pain scores and WOMAC scores for joint function using both the EITBM acupoints and the classical-consensus acupoints, but effects of the EITBM acupuncture were significantly greater than that of the classical acupuncture. Both groups also had significant increases in ROM and a reduction in serum IL-1ß, TNF-a, and MMP-13, with the EITBM acupuncture again providing significantly greater improvements.

The current study had some limitations. Unfortunately, the current study didn't evaluate the effects of exercise alone in comparison with exercise plus acupuncture and remains to be further investigated in the future.

CONCLUSIONS

Acupuncture, in combination with exercise, can relieve symptoms, improve joint function, and reduce pro-inflammatory cytokines (IL-1ß and TNF-a) as well as MMP-13 for patients with KOA. The outcomes for acupuncture using EITBM acupoints were significantly better than those of the acupoints selected using classical consensus.

AUTHORS' DISCLOSURE STATEMENT

The National Key Research and Development Plan Key Special Program of TCM Modernization Research (No. 2018YFC1707803), the Key Project of Hebei Provincial Administration of Traditional Chinese Medicine (No. Z2022009), and the General Project of Scientific Research Plan of Hebei Administration of Traditional Chinese Medicine (No. 2022057) funded the study. The authors declare there is no conflict of interest in this study.

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