

Acupuncture for symptom management of rheumatoid arthritis: a pilot study

Hyangsook Lee · Ji-Young Lee · Yun-ju Kim ·
Sehyun Kim · Changshik Yin · Jae-Ho Khil ·
Kirok Kwon · Sun-Mi Choi · Hyejung Lee ·
Hi-Joon Park

Received: 24 October 2007 / Revised: 6 December 2007 / Accepted: 6 December 2007 / Published online: 10 January 2008
© Clinical Rheumatology 2007

Abstract We investigated the feasibility of a future acupuncture trial in the symptom management of rheumatoid arthritis (RA). Twenty-five patients meeting the American College of Rheumatology (ACR) criteria were recruited and given 14 sessions of individualised acupuncture treatment for 6 weeks. Improvement in symptoms was assessed using

ACR 20, 50 and 70; disease activity score (DAS28); tender joint count; swollen joint count; morning stiffness and health-related quality of life using the Korean Health Assessment Questionnaire and the SF-36 at baseline and after 6 weeks. Erythrocyte sedimentation rate (ESR) was also assessed. At 6 weeks, 44%, 20%, and 12% of patients achieved ACR 20, 50 and 70 responses, respectively. Acupuncture also produced statistically significant improvements in DAS28, pain and global activity, swollen joint count, health-related quality of life (SF-36) and ESR. No major acupuncture-related adverse events were reported. Acupuncture treatment as used in this pilot study was safe and well-tolerated. The use of acupuncture for symptom management in RA warrants further investigation.

H. Lee · K. Kwon
College of Korean Medicine, Sangji University,
Wonju, Korea

H. Lee · C. Yin · H. Lee · H.-J. Park
Acupuncture and Meridian Science Research Centre,
Kyung Hee University,
Seoul, Korea

J.-Y. Lee · H. Lee · H.-J. Park (✉)
Department of Meridian and Acupuncture,
College of Korean Medicine, Kyung Hee University,
1 Hoegi-dong, Dongdaemoon-gu,
130-701 Seoul, Korea
e-mail: acufind@khu.ac.kr

Y.-j. Kim
Department of International Cooperation,
Ministry of Health and Welfare,
Seoul, Korea

S. Kim
Graduate School of East–West Medical Science,
Kyung Hee University,
Yongin, Korea

J.-H. Khil
College of Physical Education, Kyung Hee University,
Yongin, Korea

S.-M. Choi
Department of Medical Research,
Korea Institute of Oriental Medicine,
Daejeon, Korea

Keywords ACR 20 · Acupuncture · Disease activity · Rheumatoid arthritis

Introduction

Acupuncture is a non-pharmacological therapy in which thin needles are inserted into the body at specific spots called acupuncture points and usually manipulated to elicit a so-called deqi sensation. It has long been practiced in East-Asian countries including China, Korea and Japan for treating a variety of medical conditions. Traditionally, it is believed that acupuncture works by harmonising Qi and blood flow through the human body.

Acupuncture has been sought by patients with rheumatoid arthritis (RA) for symptomatic treatment. Although the underlying mechanism responsible for acupuncture's therapeutic effect is not well understood, accumulated evidence suggests that it has analgesic and anti-inflammatory effects. Extensive studies have been performed to support the

hypothesis that endogenous opioids are released by acupuncture [1], and electroacupuncture has been reported to suppress peripheral inflammation via a peripheral opioid mechanism in various animal inflammation models [2, 3]. While acupuncture to alleviate pain and improve function in patients with osteoarthritis has received much attention [4], little is known about the role of acupuncture in RA.

A recently updated systematic review includes only two randomised clinical trials (RCTs), which were judged to be of poor or medium quality [5]. The poor reporting and inadequate outcome measures of one study using electroacupuncture weakened the validity of its positive results [6]. In the other study, which used a crossover design, one acupuncture point on the dorsum of the foot was stimulated bilaterally for 4 min once a week for 5 weeks, which is a highly questionable application [7]. The fundamental difference in acupuncture interventions between the aforementioned studies demonstrates the lack of standardisation and accordingly, the difficulties in applying adequate techniques to properly test its effect, if any.

In the present article, we report the results of our pilot study of individualised acupuncture for the symptomatic treatment of RA to determine whether further research is warranted.

Materials and methods

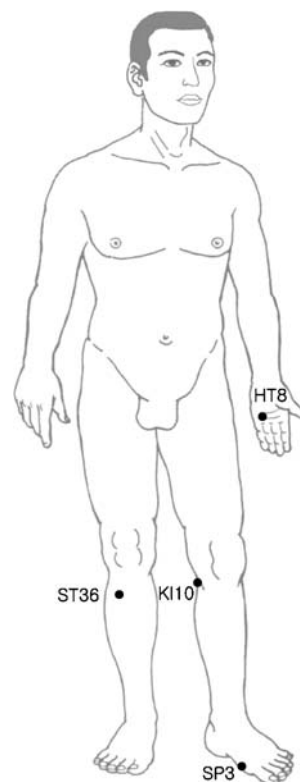
Study design and patient recruitment

The study was conducted in the Department of Acupuncture and Meridian, College of Korean Medicine, Kyung Hee University. This was a pilot, before-and-after comparison of 14 sessions of acupuncture treatment during 6 weeks in patients with RA. This study was carried out under the review of an ethics committee made up of doctors and a religious scholar. Since a formal ethics committee of our college was not established at the time of this study, we assessed the appropriateness of the protocol by consulting with the senior college staffs consisting of medical doctors, a nurse, and a priest. Patients were recruited by means of local newspaper and university website advertisements. Each patient included in the study gave written informed consent. Patients were included if they were 18–70 years old and met the American College of Rheumatology (ACR) criteria for RA [8]. The participants' RA medication regimen, if they were receiving any, was stable for the past 3 months before entry into and throughout the study. Exclusion criteria were pregnancy, breastfeeding, bleeding or coagulation disorders, skin infections, uncontrolled or ill-controlled blood pressure with diastolic pressure ≥ 110 mmHg, any other acupuncture treatment or herbal medication for RA within 3 months before screening, and needle phobia.

Acupuncture treatment

To reflect the usual practice in Korea, the acupuncture prescription was individualised based on the five elements principle in Sa-am acupuncture. Sa-am acupuncture, one of the traditional Korean acupuncture styles, uses five Shu acupuncture points under elbows and knees to treat diseases. According to its theory whereby symptoms of tender and swollen joints of RA patients are deemed to result from overheat and excessive dampness, the coupled basic acupuncture points, i.e. HT8 and KI10 to control heat and water balance or SP3 and ST36 for dampness control were basically used (Fig. 1). Acupuncture needles were given to the unaffected or less affected side. If both sides were equally painful, acupuncture was given on the left-hand side for men and on the right-hand side for women. Considering the patient's symptoms, two or three predefined acupuncture points were added from the pool of acupoints (LR8, LR2, SP2, LR1, SP1, SI5, ST41, GB41, ST43, SI3, BL66, SI2, LU8, KI7, SP3, and KI3). A few trigger or ouch points were stimulated if necessary. Number of needles inserted varied from four to nine and the depth of insertion was determined as 0.2 to 1.5 cm based on the location of the acupuncture points and the patient's symptoms. During manipulation, the deqi response was sought, after which the needles were retained for 20 min. Dis-

Fig. 1 The locations of acupuncture points used as basic prescription for acupuncture treatment



posable stainless steel needles (0.25×30 mm, DongBang Acupuncture Inc., Chungnam, Korea) were used. Treatment was given by a Korean Medicine Doctor (KMD) who was familiar with Sa-am acupuncture and had more than 3 years of clinical experience. The acupuncture treatment was given three times per week for the first 2 weeks and twice weekly for the following month [9–11].

Outcome assessments

Outcome assessment was performed by a physician who otherwise was not involved in the study. The outcome assessor was instructed to minimise conversations with the patients, and the data were analysed by a blinded statistician. Outcome measures included proportions of ACR 20, ACR 50 and ACR 70 responders; disease activity score (DAS28); tender joint counts (total 28); swollen joint counts (total 28); and morning stiffness. The ACR 20 reflects 20% improvement in tender or swollen joint counts as well as 20% improvement in three of the five parameters, i.e. patient assessment, physician assessment, erythrocyte sedimentation rate (ESR), pain scale and functional questionnaire [12]. The DAS28 was calculated using tender joint counts, swollen joint counts, ESR and patient global activity assessment [13]. For health-related quality of life, the Korean Health Assessment Questionnaire (KHAQ) and SF-36 were used, and the ESR was also measured. ACR 20 and DAS 28 were regarded as primary outcomes for this study. Adverse events (AEs) were monitored with an open question at every treatment.

Statistical analysis

Data are presented as means±SD unless stated otherwise. All statistical tests were performed using Statistical Package for the Social Sciences (SPSS; Windows version 11.0; SPSS Inc., Chicago, IL, USA). For before-and-after comparisons, Wilcoxon's signed-ranks test was used, with a *p*-value less than 0.05 regarded as significant. Dichotomised data regarding medication were analysed using the χ^2 test.

Results

Characteristics of the patients

Initially, 25 patients meeting the inclusion criteria were given 14 sessions of individualised acupuncture treatment for 6 weeks; two dropped out because of a traffic accident and travel time considerations. The baseline characteristics for the 23 patients who remained in the study are shown in Table 1.

Outcomes

Eleven patients achieved ACR 20 responses (48%) after 6 weeks. Five patients (22%) were ACR 50 responders, of whom three (13%) achieved ACR 70 responses (Table 2). Dichotomising the data into medicated and non-medicated, we found no significant difference in ACR 20 responders between patients who were receiving medication and those who were not; five of 12 (41.7%) who received medication achieved ACR 20 responses, while 6 of 11 (54.5%) who did not receive medication did so (*p*=0.435).

The mean (±SD) DAS28 score at the start of acupuncture treatment (week 0) was 4.1 (±1.0) but a significant drop occurred 6 weeks later (3.1±1.1, *p*<0.001, Table 2).

Patients reported significant improvements in both pain intensity (53.9±20.5 vs. 38.8±27.7, *p*=0.004) and global activity (59.0±17.3 vs. 40.5±28.5, *p*=0.001), as did the physicians (for pain, 34.2±16.6 vs. 23.7±14.0, *p*=0.01; for global activity, 35.5±22.9 vs. 17.9±11.9, *p*<0.001). The number of swollen joints (total 28) significantly decreased (5.2±3.5 vs. 1.4±1.9, *p*<0.001), but no significant improvement occurred in tender joint count (5.9±4.2 vs. 4.0±4.0, *p*=0.099). Morning stiffness decreased (2.0±2.3 vs. 1.4±1.7 h, *p*=0.036).

For function and quality of life assessed using the SF-36, total (40.2±17.1 vs. 47.3±16.5, *p*=0.012), physical (38.0±17.1 vs. 44.0±17.7, *p*=0.042) and mental (42.4±18.3 vs. 50.7±18.1, *p*=0.01) component scores significantly improved. The score of KHAQ was decreased but not significantly (0.8±0.6 vs. 0.6±0.6, *p*=0.054). The ESR level significantly changed from 18.3 (±14.4) to 13.3 (±14.7) after acupuncture treatment (*p*=0.024; Table 3).

All reported acupuncture-related AEs were mild: nausea (*n*=1), dizziness (*n*=1), slight fever (*n*=1) and shortness of vigour (*n*=9).

Discussion

Our preliminary findings suggest that 14 sessions of acupuncture treatment constitute a safe and potentially

Table 1 Demographic and clinical characteristics of the 23 patients

Baseline characteristics of patients	Mean (SD)
Age (yr)	52.0 (7.5)
Body mass index	22.2 (3.6)
Gender (male:female)	4:19
Acupuncture experience (naïve:experienced)	7:16
Medication (yes:no)	12:11
Duration of disease (yr)	8.4 (7.6)
Rheumatoid factor ^a (positive:negative)	13:9 ^a

Data are mean (SD), or number of patients.

^aData are from 22 patients.

Table 2 Changes in main outcome measures from the baseline in the 23 patients treated with acupuncture

	Baseline	Post-treatment	Δ	<i>P</i> -value
ACR response	Proportion of ACR 20 responders (%)	11 (48%)		
	Proportion of ACR 50 responders (%)	5 (22%)		
	Proportion of ACR 70 responders (%)	3 (13%)		
DAS28	4.1 (1.0)	3.1 (1.1)	-1.0	<0.001

ACR responses are expressed as number of patients (%), and DAS28 are mean (SD)

Δ Absolute change, *P*-value comparison between baseline and at 6 weeks by Wilcoxon's signed-ranks test

promising therapy that helps patients to manage the symptoms of RA. No patient was withdrawn from the study because of its lack of efficacy, and all patients complied with treatments as scheduled. Moreover, the treatment procedures were well-tolerated and acupuncture-related AEs were all mild and negligible.

Clinical trials evaluating the efficacy of disease-modifying antirheumatic drugs or biological agents often include patients with *active* disease, such as six or more swollen joints, six or more tender joints, an ESR of 28 or more, and/or morning stiffness of 45 min or more [14], thus, compromising the generalisability of the results. In the present study, we simply included patients meeting the ACR criteria for RA [8] because it would have been unethical or inappropriate to give acupuncture treatments to patients with active RA without our own pilot data. Furthermore, clinical trials involving participants who were not representative of the patients seen in standard clinical care have been criticised [15]. If we had adopted

the usual extensively selective inclusion criteria, 20 out of 25 participants would have been excluded from our study, and our study patients would not have been representative of RA patients commonly seen in the acupuncture clinics.

Forty-eight percent of ACR 20 responders at 6 weeks may not be an impressive result in an uncontrolled study. The participants, however, had relatively moderate or lower disease activities, (i.e. baseline DAS28 4.1 ± 1.0) compared to those included in previous RCTs of RA. Forty-eight percent of the patients were receiving only acupuncture for RA, and the medication was stable in the other 52%. Thus, our finding of 48% regarding ACR 20 responders is worthy of attention.

It is unclear whether acupuncture alleviates symptoms by expectation only or it actually decreases disease activity. After acupuncture treatment, patients in our study reported a better quality of life, as assessed by the SF-36. We also examined disease activity, and the mean DAS28 score dropped significantly after 6 weeks of acupuncture treatment. As DAS28 change is regarded as clinically relevant only when it falls below 2.6 or at least 3.2 [16], indicating remission or low disease activity, our results (DAS28 at 6 weeks, 3.1 ± 1.1) may only indicate marginal change. Swollen joint count, ESR and patient global health all improved significantly, while tender joint counts were similar throughout the study. Previous studies generally reported pain relief, but the most outstanding improvement in our results was a decrease in swollen joint count, which might reflect the anti-inflammatory effects of acupuncture, as have been reported in other studies [17, 18]. Given that the assessor was not involved in the study, the swollen joint count change is impressive, suggesting the feasibility of further investigation into the possible mechanism.

Recently, a large-scale RCT for osteoarthritis demonstrated a specific effect of acupuncture over placebo and an education control [19]. We have no knowledge whether this

Table 3 Changes in symptoms, quality of life, and laboratory tests from the baseline in 23 patients treated with acupuncture

		Baseline	Post-treatment	<i>P</i> -value
Pain score on a 100 mm VAS	Patient	53.9 (20.5)	38.8 (27.7)	0.004
	Physician	34.2(16.6)	23.7 (14.0)	0.010
Global status on a 100 mm VAS	Patient	59.0 (17.3)	40.5 (28.5)	0.001
	Physician	35.5 (22.9)	17.9 (11.9)	<0.001
No. of tender joints (0–28 joints)		5.9 (4.2)	4.2 (4.0)	0.099
No. of swollen joints (0–28 joints)		5.2 (3.5)	1.4 (1.9)	<0.001
Morning stiffness (h)		2.0 (2.3)	1.4 (1.7)	0.036
KHAQ Disability index (0–3)		0.8 (0.6)	0.6 (0.6)	0.054
SF-36	Physical health	38.0 (17.1)	44.0 (17.7)	0.042
	Mental health	42.4 (18.3)	50.7 (18.1)	0.010
	Total	40.2 (17.1)	47.3 (16.5)	0.012
ESR (mm/h)		18.3 (14.4)	13.3 (14.7)	0.024

Data are mean (SD)

KHAQ Korean health assessment questionnaire, from 0 no difficulty to 3 unable to do activity, *P*-value comparison between baseline and at 6 weeks by Wilcoxon's signed-ranks test

would be the case for RA as well. Few data exist to support acupuncture treatment in the symptom management of patients with RA [5]. Previous reports failed to demonstrate any impact on symptom improvement, ESR or C-reactive protein [6, 7].

Given that previous trials are open to criticism regarding their research methodology, our study team faced several challenges. The paucity of previous studies has created difficulty in determining the optimal intervention details, i.e. the style of acupuncture, manipulation method, number of sessions and treatment period. Little information is available on what outcome measurements would be suitable for assessing the effect of acupuncture. After a survey of experts and careful review of the literature, our acupuncture protocol was developed mainly based on Korean style acupuncture and the treatment was given by one KMD who was familiar with this style. We also included various measures frequently used in clinical trials to allow assessment of a range of possible effects of acupuncture treatment.

Given the uncontrolled nature of the study, it is difficult to draw any firm conclusions regarding the efficacy of the acupuncture treatment. The symptom improvements could either be due to acupuncture treatment itself, or natural course of the disease, or regression toward the mean. Considering the chronicity of the disease (mean 8.4 years) and moderate disease activity (mean DAS28, 4.1), however, acupuncture may have played a role in their symptom changes. The number of patients involved was small, and the duration of acupuncture treatment may not have been long enough to reflect actual practice. Another weakness of our study, mainly due to lack of funding, is that long-term follow-up assessments were not included, which might have indicated how long the benefit of acupuncture would persist after 6 weeks. Nevertheless, based on the present data, further investigation is warranted into acupuncture's role in managing the symptoms of RA patients who are not willing to accept or react adversely to conventional pharmacological treatment, or who are seeking additional benefits through unconventional combination therapeutics.

Acknowledgements This study was supported by the Acupuncture, Moxibustion and Meridian Research Project of Korea Institute of Oriental Medicine in 2005.

References

- Han JS (2004) Acupuncture and endorphins. *Neurosci Lett* 361:258–261
- Zhang GG, Yu C, Lee W, Lao L, Ren K, Berman BM (2005) Involvement of peripheral opioid mechanisms in electroacupuncture analgesia. *Explore (NY)* 1:365–371
- Kim HW, Roh DH, Yoon SY et al (2006) The anti-inflammatory effects of low- and high-frequency electroacupuncture are mediated by peripheral opioids in a mouse air pouch inflammation model. *J Altern Complement Med* 12:39–44
- White A, Foster NE, Cummings M, Barlas P (2007) Acupuncture treatment for chronic knee pain: a systematic review. *Rheumatology (Oxford)* 46:384–390
- Casimiro L, Barnsley L, Brosseau L et al (2005) Acupuncture and electroacupuncture for the treatment of rheumatoid arthritis. *Cochrane Database Syst Rev* CD003788
- Man SC, Baragar FD (1974) Preliminary clinical study of acupuncture in rheumatoid arthritis. *J Rheumatol* 1:126–129
- David J, Townsend S, Sathanathan R, Kriss S, Dore CJ (1999) The effect of acupuncture on patients with rheumatoid arthritis: a randomized, placebo-controlled cross-over study. *Rheumatology* 38:864–869
- Arnett FC, Edworthy SM, Bloch DA et al (1988) The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum* 31:315–324
- Choi S (1993) *Neijing pathology*. Log, Seoul
- Kim D (2001) *The true story of Sa-am acupuncture*. Seoklim, Seoul
- Park S, Park H, Lee H, Son Y, Lim S, Lee H (2001) A study on the concept of the right and the left in oriental medicine. *Kor J Meridian Acupoint* 18:81–94
- Felson DT, JJ, Boers M, Bombardier C, Furst D, Goldsmith C et al (1995) Preliminary definition of improvement in rheumatoid arthritis. *American College of Rheumatology. Arthritis Rheum* 38 (6):727–735
- Prevoe MLL, van't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LBA, van Riel PLCM (1995) Modified disease activity scores that include twenty-eight-joint counts: development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Rheum* 38:44–48
- Sokka T, Pincus T (2003) Most patients receiving routine care for rheumatoid arthritis in 2001 did not meet inclusion criteria for most recent clinical trials or American college of rheumatology criteria for remission. *J Rheumatol* 30:1138–1146
- Pincus T, Sokka T (2004) Should contemporary rheumatoid arthritis clinical trials be more like standard patient care and vice versa. *Ann Rheum Dis* 63(Suppl 2):ii32–ii39
- Prevoe ML, van, t Hof MA, Kuper HH, van Leeuwen MA, van de Putte LB, van Riel PL (1995) Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Rheum* 38:44–48
- Yim YK, Lee H, Hong KE et al (2007) Electro-acupuncture at acupoint ST36 reduces inflammation and regulates immune activity in collagen-induced arthritic mice. *Evid Based Complement Alternat Med* 4:51–57
- Baek YH, Choi DY, Yang HI, Park DS (2005) Analgesic effect of electroacupuncture on inflammatory pain in the rat model of collagen-induced arthritis: mediation by cholinergic and serotonergic receptors. *Brain Res* 1057:181
- Berman BM, Lao L, Langenberg P, Lee WL, Gilpin AM, Hochberg MC (2004) Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: a randomized, controlled trial. *Ann Intern Med* 141:901–910