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Comparison of ankylosing spondylitis treatment efficacy between distal and proximal point acupuncture combined with drug treatment: a randomized controlled study

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Abstract

Background: Multiple meta-analyses have found that acupuncture combined with drug treatment can effectively improve the efficacy of clinical treatment for ankylosing spondylitis. The efficacy of acupuncture is based on nearby action and/or remote action, and there have been very few studies comparing the efficacy of these two actions in the treatment of active ankylosing spondylitis. Therefore, we designed this study to observe the clinical efficacy of different acupuncture methods combined with drug treatment for ankylosing spondylitis.

Methods: Sixty patients with active ankylosing spondylitis were randomized into a test group and a control group. In addition to basic treatment with nonsteroidal anti-inflammatory drugs and empirical formula of Chinese medicine named heat-clearing, Yin-nourishing, and dehumidifying pills, the test group mainly adopted distal point acupuncture with needles manipulated once every 10 minutes and retained for 30 minutes at each of the nine acupoints, including Houxi (SI3), Shugu (BL65), Sigu (LI4), Quchi (LI11), Yanglingquan (GB34), Shenmai (BL62), Sanyinjiao (SP6), Taixi (KI3), and Zusanli (ST36), for five consecutive days per week (two days of rest per week) for two consecutive weeks. The control group mainly adopted proximal and local point acupuncture with needles manipulated once every 10 minutes and retained for 30 minutes at each of the six acupoints, including Jiaji (EX-B2), Dazhui (DU14), Tianzhu (BL10), Dachangshu (BL25), Shenshu (BL23), and Yaoyangguan (DU3), for five consecutive days per week (two days of rest per week) for two consecutive weeks. Changes between pretreatment and posttreatment ankylosing spondylitis disease activity score, McGill score, and Bath score were evaluated.

Results: Ankylosing spondylitis, McGill, and Bath score were lower in both groups with a more significant drop in the test group. After the treatments were discontinued, ankylosing spondylitis, McGill, and Bath scores were lower for the test group compared to those immediately after the two-week treatment. For the control group, ankylosing spondylitis and McGill scores were higher compared to those immediately after the two-week treatment but lower than the pretreatment scores; the Bath score was lower compared to that immediately after the two-week treatment. The differences between the two groups were statistically significant (P < 0.05).

Conclusion: Though both distal point and proximal point acupuncture combined with drug treatment can improve disease symptoms in patients with ankylosing spondylitis, the distal acupuncture group had higher and longer-lasting clinical efficacy.

Keywords: ankylosing spondylitis; proximal acupoint; distal acupoint; randomized controlled trial; ankylosing spondylitis score; McGill score
Tradition
Although no disease named ankylosing spondylitis was recorded in ancient traditional Chinese medicine books, ankylosing spondylitis should belong to the category of “Bi Zheng” (Bi syndrome) in traditional Chinese medicine according to its clinical manifestations and pathological sites in the body. Lower back pain is one of the main clinical manifestations of ankylosing spondylitis, and acupuncture has shown good clinical efficacy. Acupoints can generally be categorized into local points (acupoints in the local site of pathological changes and the surrounding area) and distal points (acupoints distal to the site of pathological changes). These two types of acupoints demonstrate nearby action and remote action of acupuncture, respectively. The chapter on contralateral needling in Yellow Emperor’s Inner Classic: Plain Questions, compiled in the Han Dynasty (202 B.C.E.–220 C.E.), noted that “The symptoms can be immediately relieved by pressing down along both sides of the spine starting from the neck and puncturing three acupoints around the site where the patient senses pain.” And this is deemed as the earliest evidence in the literature that explicitly proposed local point acupuncture (i.e., nearby action) in the treatment of lower back pain. Shu (stream) acupoints are located at the ends of the extremities. Classic of Questioning, compiled by Qin Yueren from the Han Dynasty, noted that “The Shu (stream) acupoints are punctured mainly to relieve joint pain and improve mobility.” This is the theoretical foundation for modern distal point acupuncture (remote action) in the treatment of lower back pain.

Background
Ankylosing spondylitis (AS) is a type of immune mediated inflammatory arthritis and a basic type of spondyloarthropathies [1]. A recent retrospective epidemiological study [2] showed an AS incidence of 0.29% in China, along with an increasing trend. AS mainly affects the axial skeleton, causes severe chronic pain and disability, significantly lowers quality of life, and brings immense economic burden to patients, their families, and the society [3]. Nonsteroidal anti-inflammatory drugs (NSAIDs) and tumor necrosis factor (TNF) inhibitors are the main drugs used to treat this disease. Some patients with AS have to discontinue drug treatment due to obvious hepatic and renal dysfunction caused by long-term oral administration of NSAIDs. Although newly developed biologics treatments cause less impairment to hepatic and renal functions, they significantly increase the risk of infections with Mycobacterium tuberculosis and other infections; hence, its long-term standardized application is limited to a small group of patients [4]. These issues that need to be considered in drug treatment schemes.

In recent years, clinical researchers have found that traditional acupuncture has bright prospects for clinical application. The efficacy and superiority of acupuncture combined with other therapies in the treatment of AS have also been evaluated and verified in multiple meta-analyses [5-7]. Systemic evaluation and analysis of relevant studies on the treatment of AS with acupuncture by scholars outside China [8] have shown that compared with relief drugs including salicylazosulfapyridine and methotrexate, acupuncture therapy can further improve clinical efficacy, lower the erythrocyte sedimentation rate (ESR) level (response rate: 30%–70%), and can further improve the parameters including occuput-wall distance, activity of thorax, and the finger-to-floor distance (response rate: 20%–73%), which is roughly in line with the study results of Chinese scholars [9]. Our preliminary research showed that, with lower back pain score and ESR or C-reactive protein (CRP) level improvement as the main criteria for therapeutic effects, oral administration of sustained-release diclofenac tablets combined with distal point acupuncture has a response rate of approximately 75%, and oral administration of sustained-release diclofenac tablets combined with proximal point acupuncture has a response rate of approximately 40% (the trial results have yet to be published).

Acupoints can generally be categorized into local points (acupoints in the local site of pathological changes and the surrounding area) and distal points (acupoints distal to the site of pathological changes). These two types of acupoints demonstrate the nearby action and remote action of acupuncture, respectively. Lower back pain is one of the main clinical manifestations of AS, and acupuncture therapy offers good clinical efficacy. Studies by some scholars [10] demonstrated a response rate of more than 80% in both local point acupuncture and distal point acupuncture. The chapter on contralateral needling in Yellow Emperor’s Inner Classic: Plain Questions [11], compiled in the Han Dynasty (202 B.C.E.–220 C.E.), noted that “The symptoms can be immediately relieved by pressing down along both sides of the spine starting from the neck and puncturing three acupoints around the site where the patient senses pain.” And this is deemed as the earliest evidence in literature that explicitly proposed local point acupuncture (i.e., nearby action) in the treatment of lower back pain. Shu (stream) acupoints are located at the ends of the extremities. Classic of Questioning [12], compiled by Qin Yueren from the Han Dynasty, noted that “The Shu (stream) acupoints are punctured mainly to relieve joint pain and improve mobility.” This is the theoretical foundation for modern distal point acupuncture (remote action) in the treatment of lower back pain [13]. The Great Compendium of Acupuncture and Moxibustion (1601 C.E.) compiled by Yang Jizhou from the Ming Dynasty noted that “Puncturing Weizhong (BL40) acupoints can relieve pain.” This is also evidence of remote action in acupuncture [14]. Both nearby action and remote action can relieve discomfort for patients, and a combination of local acupoints and distal acupoints is commonly used by acupuncturists in clinical practice. Studies by Miu et al. [15] proved that fire needling was an effective therapy for knee osteoarthritis in clinical practice, and distal point acupuncture (i.e., balance needle acupuncture combined with local point acupuncture) could relieve arthralgia in patients more effectively than acupuncture at local joint acupoints. However, studies by some other scholars found that distal point acupuncture combined with acupuncture at local joint acupoints offered similar therapeutic effects in alleviating arthralgia as monotherapy acupuncture at local joint acupoints [16]. Diverse study results from different researchers have demonstrated that not all local point or distal point acupuncture methods are inferior to combinations of local and distal acupoints in terms of clinical efficacy. Studies by Zhao et al. [17] found that for patients with spasms after a stroke, acupuncture at mostly distal points in the acute phase was superior to acupuncture at mostly proximal points in relieving limb spasticity, while acupuncture at mostly proximal points in the chronic phase was superior to distal point acupuncture in improving limb mobility. This result was roughly in line with conclusions made by Sun et al. in their studies on acupuncture therapy for periarticulars of the shoulder [18]. These study results indicated that proximal point acupuncture and distal point acupuncture do not offer the exact same clinical efficacy in different phases of the same disease.

One of the main clinical manifestations of AS is lower back pain characterized by alleviation after activity, exacerbated symptoms after rest, apparent nighttime manifestation, difficulty turning over in bed, and waking up with pain at night in severe cases, which is especially evident for patients with active AS disease [19]. Jiaji (EX-B2) acupoint is a typical proximal point commonly selected in the clinical treatment of AS. Some researchers [20] have found that the deep anatomical site of EX-B2 is mostly located at the intervertebral foramen where the nerve roots exit the spine, and unskilled acupuncturists might hurt the spinal nerves and cause more severe consequences. Moreover, acupuncture at the EX-B2 acupoint generally requires the patient to lie in the lateral or prone position, but for patients with active AS, extended time lying in bed tends to significantly exacerbate pain and
makes acupuncture therapy difficult to tolerate. Some studies suggest that [21] acupuncture can change the static tension of paravertebral muscles and achieve anti-inflammatory and analgesic effects; however, for patients with active inflammation, local irritation may exacerbate the inflammatory response, leading to worsening pain despite improvement of blood circulation and accelerated metabolism of inflammatory mediators [22]. However, it takes a relatively long time to achieve pain relief, so an exacerbated inflammatory response often makes it hard for the patient to adhere to treatment with acupuncture monotherapy. The 2019 International Guidelines on Treatment for Ankylosing Spondylitis [23] also pinpoint that physiotherapies, including local massage and acupuncture, are not recommended for active AS due to possible exacerbation of local inflammatory response. Acupuncture at distal acupoints, mostly located at the end of the limbs, causes no damage to the joint and enables relatively flexible selection of acupoint positions. In clinical practice, we found that distal point acupuncture (i.e., remote action) offered better therapeutic effects in the treatment of active AS. Therefore, this study, mainly conducted on patients with active AS disease activity, used local point acupuncture or distal point acupuncture combined with drug treatment as the main interventions, adopted a randomized controlled trial as the study method, and measured the results with indices, including ankylosing spondylitis disease activity score (ASDAS), Bath score, and McGill pain index, in order to compare the clinical efficacy of local point acupuncture and distal point acupuncture and potentially provide clinical evidence for treatment schemes that combine different acupuncture therapies with drug treatment.

Data and methods

General data
A total of 60 patients were enrolled from the outpatient clinic and in-patient division of the Department of Rheumatology, Beijing Hospital of Traditional Chinese Medicine, Capital Medical University from June 2019 to December 2020. Due to the higher incidence of AS and more severe symptoms in men than in women, the ratio of male patients with AS to female patients with AS in this hospital was approximately 30:1; hence, all patients enrolled in this study were male. Enrolled patients were randomized into the test group and the control group with 30 subjects in each group. Random numbers were generated in Microsoft Excel 2003, and each study subject was assigned a number from 1 to 60. Odd numbered subjects were included in the test group whereas even numbered subjects were included in the control group. Subjects were randomized by third party personnel, and doctors responsible for collecting study subjects were not involved in the randomization process. The generated random numbers, grouping details, and treatment methods were kept in sealed and opaque envelopes. Grouping details determined by the aforementioned method could not be changed. Subjects in both groups opened the sealed envelopes in sequence of inclusion, and doctors followed the treatment methods indicated in the envelopes to treat the subjects. This study was approved by the Ethics Committee of Beijing Hospital of Traditional Chinese Medicine, Capital Medical University (approval number: 2019BL02-017-02).

Inclusion criteria
Patients who satisfied the 1984 New York Diagnostic Criteria for Ankylosing Spondylitis [24] and the Assessment of SpondyloArthritis International Society diagnostic criteria for axial spondyloarthropathy [25]. ASDAS score > 1.3 and ESR or CRP levels above two times the normal upper limits; age between 18 and 60 and able to independently read and use the scale involved in the study; having discontinued drug treatment for more than 1 month except for NSAIDs and the empirical formula of Chinese medicine named heat-clearing, Yin-nourishing, and dehumidifying pills (Figure 1); good compliance and ability to undergo treatment and various tests according to the standards.

Exclusion criteria
Pregnant and lactating women; patients with severe diseases including tumors, cardiovascular, cerebrovascular, hepatic, renal, and hematopoietic system disorders and patients with mental illness; patients with other rheumatic diseases; patients unable to comply with the treatment scheme; patients who suffered from other severe diseases during their previous use of NSAIDs; patients who participated in clinical trials of drugs or nondrugs in the past six months or patients who had not participated in clinical trials in the past six months but were still in the observation period of previous clinical trials; patients allergic to test drugs or acupuncture needles.

Sample size calculation
According to medical literature and preliminary experimental results, sample size was calculated by comparing independent sample proportions of both groups in this study. Preliminary experimental results indicated higher clinical efficacy in the test group than in the control group; so one-tailed tests were adopted with two-arm parallel groups (1:1 allocation ratio). The value of type I error α was set as 0.05, and the value of type II error β was set as 0.2, with the assurance level of 1-β (80%). P1 represents the response rate of the test group, estimated to be 75% based on test results, and P2 represents the response rate of the control group, estimated to be 40%. Sample size calculated by the PASS 11.0 software indicated that 33 patients needed to be enrolled in each group based on a need of 30 patients per group and a 10% dropout rate. A total of 70 patients were recruited in clinical practice with 10 subjects who withdrew from the study during the screening phase due to personal reasons. No other patient withdrew throughout duration of the study; thus, a total of 60 subjects underwent clinical observation.

Treatment methods
The study process was divided into two phases: a 2-week treatment period and an 8-week follow-up period. During the treatment period, subjects underwent basic treatment and acupuncture therapy. During the follow-up period, subjects only received basic treatment and were followed up once every four weeks. Adequate doses of anti-inflammatory painkillers were administered in consideration of the possibility that patients might drop out of the trial during the treatment period due to exacerbated symptoms. For the above reason, the subjects were at relatively high risk of hepatic dysfunction, so safety indices such as hepatic and renal functions were checked relatively frequently throughout the whole duration of the trial. Routine blood tests and tests of safety indices including hepatic and renal functions were performed every week during the treatment period; during the follow-up period, the aforementioned safety indices were tested every four weeks until 6 months after the end of the study.

Basic treatment
All enrolled patients were administered 25 mg enteric-coated diclofenac sodium tablets three times per day and 6 g of empirical formula of Chinese medicine named heat-clearing, Yin-nourishing, and dehumidifying pills two times per day.

Acupuncture therapy
Choice of acupuncture needles: Huatuo brand acupuncture needles (manufactured by Suzhou Medical Products Factory Co., Ltd., China) were used in the study (specifications: 0.30 × 40 mm, 5 cm).

Selection of acupoints: acupoints were selected with reference to the location of acupoints: the 1990 State Standard of the People's Republic of China.

Test group: the study team adopted acupoints recommended in The Treatment of Ankylosing Spondylitis with Traditional Chinese Medicine

Figure 1 The constituent herbs of heat-clearing, Yin-nourishing, and dehumidifying pills
[26] published in 1990 for treatment in the test group and then added or reduced acupuncture based on their clinical practice. All the selected acupoints were located away from the spine, so the acupuncture therapy adopted in the test group represented remote action. The aforementioned book was the first treatise offering a systemic introduction of AS treatment with traditional Chinese medicine and has high academic value. Acupoints: Houxi (SI3), Shugu (BL65), Shenting (LI15), Zhiyang (GB34), Shenmai (BL20), Sanyinjiao (Sp6), Taixi (Kl3), and Zusanli (ST36). Acupuncture needles were manipulated once every 10 minutes and retained for 30 minutes at each acupoint for five consecutive days per week (two days of rest per week) for two consecutive weeks.

Control group: the study team added or reduced acupoints based on acupoints recommended for AS acupuncture therapy in The Guidelines for Diagnosis and Treatment of Common Internal Diseases in Traditional Chinese Medicine [27] published by China Association of Chinese Medicine in 2008. All the selected acupoints were in proximity to the spine so the acupuncture therapy adopted in the control group represented nearby action. Acupoints: Ji jia (EX-B2), Dazhui (DU14), Tianzhu (BL10), Dachangshu (BL25), Shenshu (BL23), and Yaoyangguan (DU3). Acupuncture needles were manipulated once every 10 minutes for five consecutive days per week (two days of rest per week) for two consecutive weeks.

**Observed indices**

**Primary efficacy indices.** ASDAS [28]: the Assessment of SpondyloArthritis International Society developed this index in 2009, consisting of an evaluation of overall back pain score, patient global evaluation, duration of morning stiffness, and CRP level. With the exception of CRP level, all other variables were measured using a visual analog scale (VAS) scoring system. Subjects were evaluated before treatment began, in the 1st and 2nd weeks after the start of treatment, and in the 4th and 8th weeks after the end of the acupuncture therapy.

Notes: lower back pain, patient global evaluation, duration of morning stiffness, peripheral joint pain or swelling, and fatigue were all measured with the 10-cm VAS, ranging from 0 to 10, with 10 meaning very severe.

Calculation formula: ASDAS = 0.121 × back pain + 0.058 × duration of morning stiffness + 0.110 × patient global evaluation + 0.073 × number of painful/ swelling peripheral joints + 0.579 × ln (CRP + 1).

ASDAS < 1.3 was defined as stable disease, and ASDAS ≥ 1.3 was defined as active disease; a decrease of ≥ 1.1 in ASDAS score was considered improvement of clinical significance, and an increase of ≥ 0.9 in ASDAS score was considered exacerbation of clinical significance.

**Secondary efficacy indices.** Score on the Chinese version of Short-form McGill Pain Questionnaire [29]: developed and agreed on by experts from the Chinese Association for the Study of Pain in 2013, consisting of three parts including pain rating index (PPI), VAS, and present pain intensity (PPI).

Notes: assessment of PRI: PRI consists of 11 sensory and 4 affective pain descriptors. Each of the 11 sensory descriptors was ranked by the subject on an intensity scale of none, mild, moderate, and severe, so that the nature and intensity of pain could be evaluated. Each of the four affective descriptors was ranked by the subject on an intensity scale of none, mild, moderate, and severe, so that the emotional state of the subject could be assessed. More descriptors ranked by the subject, higher intensity, and higher score signified more severe lower back pain. Questions were posed to the patient sequentially, and the answers were recorded.

Assessment of VAS: VAS scores were recorded by making a mark on a 10-cm ruler with two end points representing 0 (no pain) and 10 (acute pain). During the test, patients were required to place a mark on the scale that corresponded to the intensity of their pain.

**Assessment of PPI:** the PPI rates pain on a scale of 0–5. Both PPI and VAS were rated and cross-referenced to make it easier for the subjects to identify and read the results and to improve the accuracy of evaluation.

Bath AS score: developed by Assessment of SpondyloArthritis International Society in 2009, including Bath AS global score (BAS-G) [28] and the Bath Ankylosing Spondylitis Metrology Index (BASMI) [28].

Subjects were evaluated before treatment, in the 1st week, in the 2nd week after the start of the treatment, and in the 4th and 8th week after the end of the acupuncture therapy.

Notes: the BAS-G was measured on a 10-cm VAS (ranging from 0 to 10, with 10 meaning very severe).

BASMI: the patient’s cervical rotation (in degrees), tragus-to-wall distance (cm), lumbar scoliosis (cm), anterior lumbar flexion (cm), and intermalleolar distance (cm) were converted into corresponding scores (0–10). BASMI = 0.2 × sum of the scores for each item.

**Statistical analysis**

Measurement data were analyzed using SPSS 20.0 statistical software and presented as mean ± standard deviation ( ± s). If the measurement data conformed to the normal distribution, analysis of variance for repeated measurement was adopted; if the measurement data did not conform to the normal distribution, nonparametric tests were performed. P < 0.05 indicated that the differences were of statistical significance.

**Results**

**Comparison of general data**

All patients enrolled in both groups were male, and the two groups were comparable with no statistically significant difference in general data including age and course of disease (P > 0.05), see Table 1.

**Comparison of primary efficacy variables**

Before treatment, ASDAS scores in both groups were basically the same, with no statistically significant difference (P > 0.05). As treatment progressed, ASDAS scores gradually decreased in both groups. Treatment method and treatment duration impacted each other. As treatment progressed during the treatment period, ASDAS scores dropped to different extents in the two groups with a more significant drop in the test group, which indicated that although disease activity was inhibited in both groups, the test group showed more effective reduction of disease activity. As treatment progressed during the follow-up period, changes in ASDAS scores varied between the two groups. ASDAS scores at each follow-up visit did not drop significantly compared with that of the previous visit in the test group but were lower than the ASDAS scores from immediately after two weeks of treatment. After the end of treatment, ASDAS scores at each follow-up visit gradually increased in the control group but were lower than the test group, which indicated that the test group showed better efficacy in improving the disease activity index. Changes in ASDAS scores of both groups were clinically and statistically significant (P < 0.05), see Table 2.

**Comparison of secondary efficacy indices**

**Comparison of McGill scores.** Before treatment, McGill scores in both groups were basically the same, with no statistically significant difference (P > 0.05); as treatment progressed, McGill scores gradually decreased in both groups with a statistically significant difference (P < 0.05).

Treatment method and treatment duration impacted each other. As treatment progressed during the treatment period, McGill scores dropped to different extents in the two groups with a more significant drop in the test group, which indicated that although pain was relieved in both groups, the test group showed higher efficacy in lowering the pain index. As treatment progressed during the follow-up period, changes in McGill scores varied between the two groups. McGill scores at each follow-up visit did not drop significantly compared with McGill scores at the end of treatment in the test group; however, they were lower than McGill scores immediately after two weeks of treatment. After the end of treatment, McGill scores at each
follow-up visit gradually increased in the control group, but were lower than those at the pretreatment level, which indicated that the test group showed more lasting efficacy in relieving pain. Changes in McGill scores of both groups were clinically and statistically significant (P < 0.05), see Table 3.

**Bath AS score.** (1) Comparison of BAS-G scores. Before treatment, BAS-G scores in both groups were basically the same, with no statistically significant difference (P > 0.05); as treatment progressed, BAS-G scores gradually decreased in both groups with statistically significant difference (P < 0.05). Treatment method and treatment duration impacted each other. As treatment progressed, BAS-G scores dropped to different extents in the two groups with a more significant drop in the test group. This indicated that although the lower back pain scale improved in both groups, the test group showed higher efficacy in reducing the lower back pain scale. Changes in BAS-G scores of both groups were clinically and statistically significant (P < 0.05), see Table 4. (2) Comparison of BASMI scores. Before treatment, BASMI scores in both groups were basically the same, with no statistically significant difference (P > 0.05); as treatment progressed, BASMI scores gradually decreased in both groups with statistically significant difference (P < 0.05).

**Table 1 General data**

| Group name | Number of subjects | Sex | Age (years) | Course of disease (years) |
|------------|--------------------|-----|-------------|--------------------------|
|            |                    |     | Minimum    | Maximum                  |
|            |                    |     | T ± s       | T ± s                    |
| Test group | 30                 | Male| 19          | 58                       |
|            |                    |     | 44.80 ± 2.23| 4.27 ± 1.07              |
| Control group | 30          | Male| 19          | 57                       |
|            |                    |     | 45.10 ± 2.18| 4.32 ± 1.13              |

**Table 2 Comparison of disease activity index of AS scores (T ± s, points)**

| Group name | Number of subjects | Pretreatment | One week after onset of treatment | Two weeks after onset of treatment | Follow-up 1 | Follow-up 2 |
|------------|--------------------|--------------|-----------------------------------|-----------------------------------|-------------|-------------|
| Test group | 30                 | 2.66 ± 0.20  | 2.32 ± 0.03<sup>a,b,c</sup>      | 2.14 ± 0.43<sup>a,b,c</sup>      | 2.08 ± 0.29<sup>a,c</sup>      | 1.79 ± 0.16<sup>a,c</sup> |
| Control group | 30        | 2.85 ± 0.18  | 2.58 ± 0.22<sup>b</sup>          | 2.29 ± 0.13<sup>a,b</sup>        | 2.39 ± 0.39<sup>c</sup>        | 2.56 ± 0.22<sup>c</sup> |

<sup>a</sup>P < 0.05 compared with pretreatment level in the same group; <sup>b</sup>P < 0.05 compared with 1 week after onset of treatment in the same group; <sup>c</sup>P < 0.05 compared with the control group at the same visit; AS, ankylosing spondylitis.

**Table 3 Comparison of McGill scores (T ± s, points)**

| Group name | Number of subjects | Pretreatment | One week after onset of treatment | Two weeks after onset of treatment | Follow-up 1 | Follow-up 2 |
|------------|--------------------|--------------|-----------------------------------|-----------------------------------|-------------|-------------|
| Test group | 30                 | 28.21 ± 6.32 | 20.28 ± 0.21<sup>a,b,c</sup>     | 14.21 ± 1.23<sup>a,b,c</sup>     | 13.02 ± 2.21<sup>a,c</sup>     | 12.89 ± 1.12<sup>a,c</sup> |
| Control group | 30       | 29.28 ± 7.03 | 26.01 ± 0.11<sup>c</sup>         | 16.42 ± 2.01<sup>a,b</sup>       | 17.89 ± 1.21<sup>c</sup>       | 20.46 ± 3.22<sup>c</sup> |

<sup>a</sup>P < 0.05 compared with pretreatment level in the same group; <sup>b</sup>P < 0.05 compared with 1 week after onset of treatment in the same group; <sup>c</sup>P < 0.05 compared with the control group at the same visit.

**Table 4 Comparison of BAS-G for lower back pain scores (T ± s, points)**

| Group name | Number of subjects | Pretreatment | One week after onset of treatment | Two weeks after onset of treatment | Follow-up 1 | Follow-up 2 |
|------------|--------------------|--------------|-----------------------------------|-----------------------------------|-------------|-------------|
| Test group | 30                 | 5.20 ± 1.02  | 3.39 ± 0.13<sup>c</sup>          | 1.91 ± 0.12<sup>a,b,c</sup>      | 1.12 ± 0.21<sup>a,c</sup>     | 0.89 ± 0.12<sup>a,c</sup> |
| Control group | 30       | 5.19 ± 1.13  | 3.98 ± 0.42<sup>c</sup>          | 2.92 ± 0.03<sup>b</sup>          | 1.89 ± 0.21<sup>c</sup>       | 1.46 ± 0.92<sup>c</sup> |

<sup>a</sup>P < 0.05 compared with pretreatment level in the same group; <sup>b</sup>P < 0.05 compared with 1 week after onset of treatment in the same group; <sup>c</sup>P < 0.05 compared with the control group at the same visit; AS, ankylosing spondylitis.

**Table 5 Comparison of BASMI scores (T ± s, points)**

| Group name | Number of subjects | Pretreatment | One week after onset of treatment | Two weeks after onset of treatment | Follow-up 1 | Follow-up 2 |
|------------|--------------------|--------------|-----------------------------------|-----------------------------------|-------------|-------------|
| Test group | 30                 | 1.69 ± 0.07  | 1.38 ± 0.14<sup>c</sup>          | 1.00 ± 0.02<sup>b,c</sup>        | 0.63 ± 0.11<sup>c</sup>     | 0.31 ± 0.02<sup>c</sup> |
| Control group | 30       | 1.71 ± 0.10  | 1.46 ± 0.08<sup>b</sup>          | 1.25 ± 0.18<sup>b</sup>          | 0.98 ± 0.14  | 0.66 ± 0.20  |

<sup>a</sup>P < 0.05 compared with pretreatment level in the same group; <sup>b</sup>P < 0.05 compared with 1 week after onset of treatment in the same group; <sup>c</sup>P < 0.05 compared with the control group at the same visit; BASMI, Bath Ankylosing Spondylitis Metrology Index.
Discussion

AS is a chronic inflammatory disease that exhibits a higher prevalence among young adults. In the advanced stages, AS can manifest with a rigid spine and joint damage, causing loss of mobility. Although the advent of biologics has greatly lowered the incidence of disability, their relatively high price and potential adverse side effects tend to make it hard for patients to adhere to treatment. Modern studies have shown that acupuncture can improve blood circulation and nutrient supply in local tissues, facilitate local metabolism, and stimulate the release of neurotransmitters (e.g., serotonin and endorphins) from nerve cells by activating the hypophysis cerebri, so that anti-inflammatory and analgesic effects can be achieved. In recent years, acupuncture therapy has been widely used in the auxiliary treatment of AS. Studies by Li et al. [7] found that acupuncture was suitable for wide application in clinical practice due to its certain advantages in the treatment of AS, including improving chest movements, lumbar range of motion, and inflammatory marker levels (ESR and CRP) in patients with AS.

AS usually belongs to the category of “Bi Zheng” (Bi syndrome) in traditional Chinese medicine. With lower back pain as one of the main manifestations of AS and the Du Mai (governing meridian) running along the middle of the back, acupuncturists have reached a broad consensus of treating AS via the governing meridian [31]. EX-B2 is a group of 34 acupoints located on the extra acupoints on both sides of the spinal column, 0.5 Cun lateral to the lower border of each spinous process, from the first thoracic vertebra to the fifth lumbar vertebra. Due to the proximity of these acupoints to the spinal column, modern medical practitioners mostly select these core acupoints based on syndrome differentiation, with good clinical efficacy. Therefore, the control group of this study adopted a combination of acupoints with EX-B2 as the core acupoints. The selected acupoints in the test group and the control group of this study represent two categories of acupuncture therapy: local point acupuncture in the control group (representing nearby action) and distal point acupuncture in the test group (representing remote action). The study results indicated that ASDAS scores, McGill scores, and Bath scores were improved in both groups, but the test group exhibited higher and more lasting efficacy in lowering disease activity and improving symptoms and joint functions.

The nearby action of acupuncture (i.e., the therapeutic effects of local point acupuncture at the local site of pathological changes and the surrounding tissues or organs) is the embodiment of the law of “stimulating the key acupoints for primary treatment” and conforms to modern ideas of anatomy. The remote action of acupuncture (i.e., stimulating the area where meridians run along for primary treatment) refers to the therapeutic effects of puncturing acupoints distal to the site of pathological changes in tissues or organs. As for acupuncture positions, distal point acupuncture is more convenient and can solve the problem of the unsuitability of needling in locally affected areas. Some studies [32] have pointed out that conventional local point acupuncture could activate the endogenous descending inhibitory systems, raise local pain thresholds, and reduce the patient’s emotional reaction to pain, so as to achieve the effect of inhibiting pain with pain. At the same time, acupuncture can block the transmission of pain signals up to the central nervous system and achieve endogenous pain inhibition [33]. By stimulating the peripheral nervous system, acupuncture therapy increases the endorphin level, intervenes in the spinal cord dorsal horn by central inhibition, blocks the release of substance P, enhances acupuncture signals, and weakens pain signals. Some clinical observations showed no significant difference in clinical efficacy between distal point acupuncture and local point acupuncture, except for an increased short-term pain inhibition in distal point acupuncture compared to local point acupuncture [34]. The reason might be that according to the relationships between anatomical entities and human body parts, the anterior central gyrus and the anterior portion of the paracentral lobule, the area that receives projections from the extremities, is larger than the area receiving projections from the trunk. Thus, manipulating acupuncture needles at distal points with the same amount of needling stimulus might offer better analgesic effects than local point acupuncture [35]. The test group of this study demonstrated a more significant drop in McGill pain scores than the control group. From the perspective of pain inhibition, these are the possible mechanisms of distal point acupuncture and local point acupuncture in achieving pain inhibition.

Studies by some scholars [36] on the treatment of cervical spondylopathy with distal point acupuncture showed that as a form of pain-inducing inflammatory substance in human body, the effects of prostaglandin E2 on intervertebral disc degeneration mainly manifest with symptoms. By inducing pain via depolarization of primary afferent neurons, a trace amount of prostaglandin E2 in the local area may be able to increase the body’s sensitivity to other pain-inducing substances. Various inflammatory factors including TNF-α and interleukin-1 can induce the activation of IkkappaB kinase beta/NF-κB. After IkkappaB kinase beta/NF-κB is activated, large quantities of inflammatory factors are produced, which immerses the intervertebral discs in a chronic inflammatory environment, promotes cell deformation and apoptosis, and causes intervertebral disc degeneration. This study demonstrated the anti-inflammatory effects of distal point acupuncture, and the aforementioned inflammatory process was found to also occur in patients with AS [3]. From the perspective of basic pathology [37], in the case of acute inflammation, more local inflammatory factors such as TNF-α are released, which significantly damages the capillaries. The penetration of a foreign body (acupuncture needle) into the body can act to stimulate the local area and result in local aggregation of macrophages and neutrophils, causing more inflammatory factors to be released and lead to aggravated inflammation. Therefore, distal point acupuncture provides higher clinical efficacy than local point acupuncture. Both groups of this study saw improvement of ASDAS scores, with a more marked drop in the test group. In clinical practice, for patients with chronic arthritis, acupuncture therapy can achieve satisfactory therapeutic effects by improving local tissue adhesion via local de-adhesion. For patients with acute inflammatory arthritis, the pain is caused by large quantities of released inflammatory factors and damaged capillaries; hence, local point acupuncture generally fails to provide satisfactory efficacy.

Despite these preliminary results, the conclusions of this study might be biased due to the small sample size in each group, high dropout rate, and all male subjects. Further studies should focus on increasing the sample size and the number of subjects, collaborating across multiple centers, and establishing more specific study groups and timeline for follow-up visits according to results of this study to further discuss the relationship between responsive subjects, treatment duration, and clinical efficacy.

Conclusion

This study found that both distal and local point acupuncture combined with drug treatment can improve the disease activity of patients with AS; and the remote action group showed clearer and more lasting efficacy in improving disease activity (i.e., ASDAS scores), clinical symptoms (i.e., McGill pain scores), and joint functions (i.e., Bath scores).

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