

Acupuncture therapy for osteoarthritis: Role and effectiveness

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Abstract

Osteoarthritis (OA), a degenerative joint disease, is the most common form of arthritis. At present, there is no cure treatment for OA. Supportive and symptomatic treatment such as pain relief and improvement of joint function are recommended. However, many pharmacologic treatments were reported to associate with significant side effects. Acupuncture is one of a promising therapy which was widely studied for OA treatment. The present review focuses on the effectiveness of acupuncture for the treatment of osteoarthritis.

Keywords: Acupuncture, osteoarthritis

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การฝังเข็มเพื่อรักษาโรคข้อเสื่อม

ลัดดา ฤกษ์ศุภผล

ภาควิชาเวชศาสตร์ป้องกันและสังคม คณะแพทยศาสตร์ มหาวิทยาลัยศรีนครินทรวิโรฒ

บทคัดย่อ

โรคข้อเสื่อม (Osteoarthritis; OA) เป็นโรคข้ออักเสบที่พบบ่อยที่สุด ในปัจจุบันยังไม่มีการรักษาใดที่ทำให้โรคหายขาด การรักษาส่วนใหญ่เป็นการรักษาตามอาการ เช่น การลดความเจ็บปวด และเพิ่มประสิทธิภาพการทำงานของข้อ อย่างไรก็ตามการรักษาด้วยยาหลายชนิดมีรายงานถึงผลข้างเคียงของการรักษาอย่างมีนัยสำคัญ การฝังเข็มเป็นอีกวิธีหนึ่งที่ใช้บำบัดโรคข้อเสื่อมที่ได้มีการศึกษาอย่างแพร่หลาย บทความนี้มุ่งที่จะทบทวนประสิทธิภาพของการฝังเข็มในการรักษาโรคข้อเสื่อม

Introduction

Osteoarthritis (OA), known as a degenerative arthritis, is the most common form of articular disease in adults worldwide. Clinical manifestations of the disease associate with the articular cartilaginous degeneration and intra-articular inflammation with synovitis resulting in changes of subchondral and peri-articular bone¹. The common affected sites of OA are hip, knees, hand, feet, and spine. Patients suffering from OA may present with limitation of joint movement, joint tenderness, muscle spasm and crepitus sensation within the joint leading to joint dysfunction and disability. Patients usually report their pain as their initiating movement and be attenuated during day. In advance stage, pain may persist over the course of disease leading to the limitation of daily activities. Not only functional impairment but emotional, mental and social functions of patient are also deteriorated.

Prevalence of OA varies depending on study population: 14-27% in States², 10-98% in Europe³⁻⁷, and 24-72% in Asia⁸⁻¹³. In Thailand, prevalence of OA ranged from 30-50%¹⁴. Treatment of OA includes both non-pharmacologic and pharmacologic therapies. Treatments of OA are usually commenced with symptomatic and supportive methods such as exercise, lifestyle modification and analgesics. In severe case, surgical interventions such as

joint replacement surgery could be used to improve quality of life. However, worrisome of medication side effects and risk of surgery, patients may try other treatment options. Acupuncture is accepted worldwide as a complementary and alternative medicine (CAM) which its effect has been promising in many diseases¹⁵. This article emphasizes on role and effectiveness of acupuncture for OA treatment.

Burden

The economic burden of OA disease is extremely high, and can divided into direct and indirect treatment cost¹⁶. About one-third of direct OA cost is contributed to medications for pain management such as non-steroidal anti-inflammatory drugs (NSAIDs), intra-articular modalities (corticosteroids and/or hylauronate), glucosamine sulfate, chondroitin sulfate, or diacerein^{17, 18}. The other half of the cost goes to hospitalization required for knee or hip replacement surgery. Indirect cost includes home care, reduced job performance, impaired performance, medical equipments and disability¹⁶.

Risk Factors

One of the leading risk factor for all types of OA is the progression of age. Other endogenous risk factors are female gender, elevated bone density, ethnicity (more common in European), family history and post-menopausal

changes. Exogenous risk factors are overweight and/or obesity, prior or repetitive trauma, work- or recreational-related activities and other lifestyle factors such as alcohol and tobacco use^{19, 20}. The various genes have been implicated for the predisposition of OA including aspirin encoding gene (ASPN), calmodulin 1 gene (CALM1), cartilage oligomatrix protein gene (COMP), Vitamin D receptor (VDR), Secreted frizzled related protein-3 (FRZB), Estrogen receptor α (ESR1), Bone morphogenetic protein-5 (BMP5), IL-1 gene cluster Interleukin-4 receptor (IL4R), Type II collagen (COL2A1), Type IX collagen (COL9A1), Matrilin-3 (MATN3) and Aggrecan (AGC1) CILP²¹⁻²⁴.

Diagnosis

Early diagnosis is the important factor for prevention of further the progression of OA. To date, there is no satisfactory treatment available for the treatment of OA. Thus, prevention rather than treatment is the most preferred approach. Apart from the history taking and physical examination, various techniques have been used for the diagnosis of OA.

Biochemical markers which helped for the diagnosis of OA include of serum hyaluronic acid, cartilage oligomeric matrix protein, cartilage glycoprotein-39 and urinary type II collagen helical peptide^{25, 26}.

Imaging studies are used both for diagnosis and to follow the progression of disease.

Plain X-ray films in both antero-posterior and lateral views should be obtained. Other routine imaging methods such as magnetic resonance imaging (MRI), ultrasoundography are the useful methods to demonstrate hyaline cartilage, soft tissue and fluid filled space^{19, 27}. ^{99m}Tc bone scanning is used to assess metabolic activity in the subchondral bone. Other diagnostic methods which are recently studied such as analyzer-based x-ray imaging (ABI) phase contrast technique²⁸, vibroarthrographic signal analysis²⁹ and 18 F-fluoride positron emission tomography³⁰.

Conventional treatment for Osteoarthritis

Up to date, OA is not a curable disease. The goal of treatment is to relieve signs and symptoms and to slow progression of disease. The conventional treatment methods include of physiotherapy, pharmacologic therapy, physiotherapy treatment, orthopedic aids and arthoses and surgery^{19,20}. Physiotherapy treatment includes ultrasound, muscle stimulation, acupuncture, heat and cold therapy etc.

The current used pharmacologic therapy includes analgesic/anti-inflammatory drugs, glucocorticoids, opioids, slow-acting drugs for osteoarthritis (SADOA) and anti-cytokines. The side effects of pharmacologic agents are highly be concerned in current management. NSAIDs are associated with gastric ulceration, nephrotoxic and cardio toxicity; while opioids are associated

with respiratory depression, impaired cognition and central apnea³¹.

The SADOA subdivided into symptomatic slow-acting drugs for osteoarthritis (SYSADOA) and disease-modifying osteoarthritis drugs (DMOAD), as suggested by Osteoarthritis Research Society International (OARSI). The symptomatic slow-acting drugs for osteoarthritis (SYSADOA) includes of chondroitin sulphate, hyaluronic acid, D-glucosamine sulphate, while disease-modifying osteoarthritis drugs (DMOAD) includes of diacerin, matrix-metalloproteinases (MMPs), glucosamine, bisphosphonates, inducible nitric oxide synthase inhibitors, doxycycline, glucosamine¹⁹. Mechanism of action is not yet elucidated, however, the inhibition of inflammation and nociceptor blockage was potentially action. Even no severe systemic side effect was reported with this medication group, the high cost for the palliative treatment is considered.

The complementary and alternative medications (CAM) in today's scenario are gaining popularity due to their safety prospects as compared to the existing drugs for OA. There were evidences that glucosamine, avocado/soybean unsaponifiables and chondroitin in osteoarthritis had positive effect and safe in reducing pain and improve function in OA patients³². Recently, acupuncture has been employed for the treatment of OA as it is

safe, cost-effective, reliable, and devoid of side effects.

Acupuncture for treatment of osteoarthritis

Overview of Acupuncture

Acupuncture is the widely practiced Chinese therapy, which utilizes needle to stimulate specific points in our body known as acupoints. In early days, bamboo and bone needles were used as a tool for acupuncture. The therapy is based on treating the causes of symptoms rather than the symptom itself³³.

Acupuncture is used for the treatment of various pain ailments such as headache, back pain, neck pain, fibromyalgia, dental pain, OA, migraine, post-operative pain, etc³⁴. Other indications for the treatment with acupuncture include chemotherapy induced nausea and vomiting, post-operative emesis, asthma, weight reduction, tinnitus, dental problems, smoking cessation, etc³³.

Theories of acupuncture

Yin-Yang theory: It is based on the concept that everything in the universe exists either in "Yin" or in "Yang" state. Yin represents coldness, stationary, dark objects, whereas Yang represents warmth, motion, light objects. Acupuncture balances the energy flow between Yin and Yang within human body³⁵.

Qi theory: Qi means vital energy of the body that flows through energy channels known

as meridians. Various factors affect Qi flow e.g. improper nutrition, emotional stress, illness, pollution etc. Therefore, acupuncture stimulates various acupoints that locate on meridians and helps to relief from the illnesses³⁶.

Gate-control and neuro-hormonal

theory: This is that, pain perception is a network between inhibitory and excitatory pathways in brain stem, thalamus, and cerebral cortex. The inhibitory pathway controls the gate on- or off-phenomenon of pain receptors and controls the release of endogenous opioid neurohormones such as enkephalin and endorphin³⁷. Functional magnetic resonance imaging (fMRI) had been used to elucidate the involvement of CNS pathway during acupuncture therapy³⁸. Wu et al³⁸ demonstrated acupoints at ST.36 (leg) and LI.4 (hand) in 90 healthy individuals and found that acupuncture stimulated autonomic nervous system and consequently caused bradycardia as a result higher scores of De-Qi effect. It was also observed that the analgesic effects by acupuncture had involved various pathways such as hypothalamic endorphinergic neurons, periaqueductal grey matter of mesencephalon, raphe nucleus, and nucleus accumbens³⁸.

Results from the recent studies

Since the US Food and Drug Administration (US FDA) accepted and classified acupuncture needles from class III (investigational

use) to class II (general acupuncture use) in 1996³⁹, acupuncture treatment was adopted to treat in various conditions such as postoperative and chemotherapy induced nausea/ vomiting, dental pain and OA¹⁵. Acupuncture treatment for OA was recommended by American College of Rheumatology (ACR)⁴⁰, however, the practice was postponed because of a lack of good evidence based studies to support. In 2008, Selfe et al⁴¹ reviewed the RCTs using acupuncture treatment for OA which published in English literatures. The literature search from 1966 to 2006 was performed which included 10 RCTs representing 1,456 OA suffering participants. The results found that pain was significantly decreased in the study group compared to the control in 8 of 10 studies. Moreover, one of these studies found that pain was significantly reduced in acupuncture group compared to diclofenac-treated group⁴². The authors suggested that the negative findings in one study should be interpreted with caution because of the flawed sham treatment⁴³. In summary, they concluded that acupuncture should be considered a viable adjunct or alternative treatment of knee OA as 9 of 10 RCTs studies reported effectiveness of acupuncture treatment. From this review, the common acupoints used for the OA treatment were ST-35 (7 studies), ST-36 (5 studies), SP-9 and GB-34 (6 studies). Others used acupoints

were ST-34, SP-6, LI-4, GB-39, BL-60, KI-3 and Xiyian⁴¹. The courses of treatment were varied from 4 to 26 weeks.

Selfe's work had supported by a systematic review and meta-analysis by Bjordal et al⁴⁴ which was published one year earlier. Bjordal did analysis for the short term efficacy of physical interventions in osteoarthritic knee pain and reported that, electro-acupuncture as well as other physical interventions such as transcutaneous electrical nerve stimulation and low level laser therapy provided clinically improvement for pain relief in OA knee.

Soon after the Selfe's report, Williamson et al⁴⁵ conducted a RCT (2007) comparing acupuncture therapy to physiotherapy or standard advice in severe knee OA awaiting arthroplasty. The outcome measures were assessed using questionnaire containing Oxford Knee Score. Acupuncture treatment was given for once a week for a total of 6 weeks. The results found that there was a significant reduction of pain in acupuncture treatment group compared to the others at the 7th week after treatment, however, these effects were no longer present at the subsequent follow-up.

The recent study by Lansdown et al⁴⁶ also supported the previous systematic review. The RCT was conducted in 30 OA suffering patients aged over 50 years comparing

“acupuncture plus usual care” to “usual care alone”. The used acupoints were SP 6, 9, and 10; ST 36; LIV 3 and 8; LI 4; GB 34 and 41; KID 6; SJ 5; and the extra point Xiyian. The results found that pain index was significantly reduction at 3 months in the acupuncture group compared to usual care group. However, the effectiveness was not sustained at 12 months which may cause from insufficiency of the study population.

The studies of acupuncture treatment for OA in non English-language articles were also frequently published. However, there were variation in study designs, clinical settings and outcome measurement among studies.

Zhu et al⁴⁷ conducted a randomized study in 124 OA suffering patients using moxibustion plus electroacupuncture (EA) compared to a diclofenac-treated group. Moxibustion was applied to Shenque (CV 8) and EA were applied at Liangqiu (ST 34), Heding (EX-LE 2), Neixiyian (EX-LE 4) for 5 sessions/ week for 10 weeks. They found that the pain scores and severity of osteoarthritis in moxibustion plus electroacupuncture (EA) were significantly decreased compared to the medication group.

Xu et al⁴⁸ studied using electroacupuncture therapy in 43 patients suffering from OA. The employed acupoints were Liangqiu (ST 34), Xuehai (SP 10) and Yinlingquan (SP 9).

They reported that, at the end of study, pain intensity was decreased and joint mobility was improved compared to the beginning. Moreover, interleukin-1 β and tumor necrosis factor α levels were decreased which considered as a mechanism of action.

The Cochrane systematic review reported from 16 RCTs which reported through 2008, involving 3,498 OA suffering patients⁴⁹. From 16 studies, 12 reported from knee OA; 3 reported from hip OA and 1 study was a mix of hip and/or knee OA. The results found that acupuncture treatment had borderline beneficially over sham acupuncture in pain reduction and functional improvement. In comparison to a waiting list control (no treatment), acupuncture had significant short-term improvement in all areas. However, acupuncture did not showed significant improvement when compared to home exercise/leaflet and supervised exercise. In the bottom line, the authors suggested that the improvement of acupuncture treatment may be due to the patients' expectation or placebo effects rather than its real efficacy.

Suarez-Almazor et al⁵⁰ had suspected and conducted a study to evaluate the placebo effect of acupuncturists' behavior on efficacy of acupuncture treatment on OA. The authors conducted a RCT in knee OA comparing acupuncture, sham acupuncture (acupuncture at

non meridian points with shallow needles). They found that there was no significant difference in pain reduction between groups. However, acupuncturists' styles had significant effects on pain reduction and satisfaction. The authors suggested that the the efficacy of acupuncture on pain reduction may cause from the placebo effects related to the acupuncturist's behavior.

Conclusion

Acupuncture shows a short-term effectiveness in pain reduction and improvement of joint function in patients with OA especially when compared with the non-treatment control group. However, these clinical effects are inconsistent among previous studies due to heterogeneity and difference in study designs. Most studies enrolled patients with OA knees but lacking of other affected joints. Moreover, large population with long-term follow up study should be considered and compared with other CAM. Study of sham and placebo effect is also required.

References:

1. Goldring MB, Goldring SR. Osteoarthritis. *J Cell Physiol* 2007;213:626-34.
2. Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. *Arthritis Rheum* 2008;58:26-35.

3. Kalichman L, Li L, Batsevich V, Malkin I, Kobylansky E. Prevalence, pattern and determinants of radiographic hand osteoarthritis in five Russian community-based samples. *Osteoarthritis Cartilage* 2010;18:803-9.
4. Fernandez-Lopez JC, Laffon A, Blanco FJ, Carmona L. Prevalence, risk factors, and impact of knee pain suggesting osteoarthritis in Spain. *Clin Exp Rheumatol* 2008;26:324-32.
5. Forestier R, Francon A, Briole V, Genty C, Chevallier X, Richette P. Prevalence of generalized osteoarthritis in a population with knee osteoarthritis. *Joint Bone Spine* 2010.
6. Horvath G, Koroknai G, Acs B, Than P, Bellyei A, Illes T. Prevalence of radiographic primary hip and knee osteoarthritis in a representative Central European population. *Int Orthop* 2010.
7. Lingard EA, Mitchell SY, Francis RM, et al. The prevalence of osteoporosis in patients with severe hip and knee osteoarthritis awaiting joint arthroplasty. *Age Ageing* 2010;39:234-9.
8. Yoshimura N, Muraki S, Oka H, et al. Prevalence of knee osteoarthritis, lumbar spondylosis, and osteoporosis in Japanese men and women: the research on osteoarthritis/osteoporosis against disability study. *J Bone Miner Metab* 2009;27:620-8.
9. Du H, Chen SL, Bao CD, et al. Prevalence and risk factors of knee osteoarthritis in Huang-Pu District, Shanghai, China. *Rheumatol Int* 2005;25:585-90.
10. Kang X, Fransen M, Zhang Y, et al. The high prevalence of knee osteoarthritis in a rural Chinese population: the Wuchuan osteoarthritis study. *Arthritis Rheum* 2009;61:641-7.
11. Kim I, Kim HA, Seo YI, Song YW, Jeong JY, Kim DH. The prevalence of knee osteoarthritis in elderly community residents in Korea. *J Korean Med Sci* 2010;25:293-8.
12. Muraki S, Oka H, Akune T, et al. Prevalence of radiographic knee osteoarthritis and its association with knee pain in the elderly of Japanese population-based cohorts: the ROAD study. *Osteoarthritis Cartilage* 2009;17:1137-43.
13. Zhang Y, Hunter DJ, Nevitt MC, et al. Association of squatting with increased prevalence of radiographic tibiofemoral knee osteoarthritis: the Beijing Osteoarthritis Study. *Arthritis Rheum* 2004;50:1187-92.
14. Tangtrakulwanich B, Geater AF, Chongsuvivatwong V. Prevalence, patterns, and risk factors of knee osteoarthritis in Thai monks. *J Orthop Sci* 2006;11:439-45.

15. NIH Consensus Conference. Acupuncture. *Jama* 1998;280:1518-24.
16. Bitton R. The economic burden of osteoarthritis. *Am J Manag Care* 2009;15:S230-5.
17. Zhang W, Moskowitz RW, Nuki G, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage* 2008;16:137-62.
18. Zhang W, Doherty M, Leeb BF, et al. EULAR evidence based recommendations for the management of hand osteoarthritis: report of a Task Force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). *Ann Rheum Dis* 2007;66:377-88.
19. Michael JW, Schluter-Brust KU, Eysel P. The epidemiology, etiology, diagnosis, and treatment of osteoarthritis of the knee. *Dtsch Arztebl Int* 2010;107:152-62.
20. Altman RD. Early management of osteoarthritis. *Am J Manag Care* 2010;16 Suppl Management:S41-7.
21. Valdes AM, Loughlin J, Oene MV, et al. Sex and ethnic differences in the association of ASPN, CALM1, COL2A1, COMP, and FRZB with genetic susceptibility to osteoarthritis of the knee. *Arthritis Rheum* 2007;56:137-46.
22. Kaliakatsos M, Tzetis M, Kanavakis E, et al. Aspirin and knee osteoarthritis in patients of Greek origin. *Osteoarthritis Cartilage* 2006;14:609-11.
23. Valhmu WB, Raia FJ. myo-Inositol 1,4,5-trisphosphate and Ca(2+)/calmodulin-dependent factors mediate transduction of compression-induced signals in bovine articular chondrocytes. *Biochem J* 2002;361:689-96.
24. Mototani H, Mabuchi A, Saito S, et al. A functional single nucleotide polymorphism in the core promoter region of CALM1 is associated with hip osteoarthritis in Japanese. *Hum Mol Genet* 2005;14:1009-17.
25. Bruyere O, Collette J, Kothari M, et al. Osteoarthritis, magnetic resonance imaging, and biochemical markers: a one year prospective study. *Ann Rheum Dis* 2006;65:1050-4.
26. Charni N, Juillet F, Garnerio P. Urinary type II collagen helical peptide (HELIX-II) as a new biochemical marker of cartilage degradation in patients with osteoarthritis and rheumatoid arthritis. *Arthritis Rheum* 2005;52:1081-90.
27. Wang YX, Griffith JF, Ahuja AT. Non-invasive MRI assessment of the articular cartilage in clinical studies and experimental settings. *World J Radiol* 2010;2:44-54.

28. Coan P, Wagner A, Bravin A, Diemoz PC, Keyrilainen J, Mollenhauer J. In vivo x-ray phase contrast analyzer-based imaging for longitudinal osteoarthritis studies in guinea pigs. *Phys Med Biol* 2010;55:7649-62.
29. Wu Y, Krishnan S, Rangayyan RM. Computer-aided diagnosis of knee-joint disorders via vibroarthrographic signal analysis: a review. *Crit Rev Biomed Eng* 2010;38:201-24.
30. Umemoto Y, Oka T, Inoue T, Saito T. Imaging of a rat osteoarthritis model using (18)F-fluoride positron emission tomography. *Ann Nucl Med* 2010;24:663-9.
31. Barron MC, Rubin BR. Managing osteoarthritic knee pain. *J Am Osteopath Assoc* 2007;107:ES21-7.
32. Pirota M. Arthritis disease - the use of complementary therapies. *Aust Fam Physician* 2010;39:638-40.
33. Kaptchuk TJ. Acupuncture: theory, efficacy, and practice. *Ann Intern Med* 2002;136:374-83.
34. Kelly RB. Acupuncture for pain. *Am Fam Physician* 2009;80:481-4.
35. Faust S. For an updated acupuncture. *Rev Med Brux* 1998;19:A290-5.
36. Vanderploeg K, Yi X. Acupuncture in modern society. *J Acupunct Meridian Stud* 2009;2:26-33.
37. Bishop B. Pain: its physiology and rationale for management. Part III. Consequences of current concepts of pain mechanisms related to pain management. *Phys Ther* 1980;60:24-37.
38. Wu MT, Hsieh JC, Xiong J, et al. Central nervous pathway for acupuncture stimulation: localization of processing with functional MR imaging of the brain—preliminary experience. *Radiology* 1999;212:133-41.
39. US Food and Drug Administration. Acupuncture needles no longer investigational. FDA Consumer. 1996. [February 4, 2006]. Available at: http://www.fda.gov/Fdac/departs/596_upd.html.
40. Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. *Arthritis Rheum* 2000;43:1905-15.
41. Selfe TK, Taylor AG. Acupuncture and osteoarthritis of the knee: a review of randomized, controlled trials. *Fam Community Health* 2008;31:247-54.
42. Sangdee C, Teekachunhatean S, Sananpanich K, et al. Electroacupuncture versus diclofenac in symptomatic treatment of osteoarthritis of the knee: a randomized controlled trial. *BMC Complement Altern Med* 2002;2:3.

43. Takeda W, Wessel J. Acupuncture for the treatment of pain of osteoarthritic knees. *Arthritis Care Res* 1994;7:118-22.
44. Bjordal JM, Johnson MI, Lopes-Martins RA, Bogen B, Chow R, Ljunggren AE. Short-term efficacy of physical interventions in osteoarthritic knee pain. A systematic review and meta-analysis of randomised placebo-controlled trials. *BMC Musculoskelet Disord* 2007;8:51.
45. Williamson L, Wyatt MR, Yein K, Melton JT. Severe knee osteoarthritis: a randomized controlled trial of acupuncture, physiotherapy (supervised exercise) and standard management for patients awaiting knee replacement. *Rheumatology (Oxford)* 2007;46:1445-9.
46. Lansdown H, Howard K, Brealey S, MacPherson H. Acupuncture for pain and osteoarthritis of the knee: a pilot study for an open parallel-arm randomised controlled trial. *BMC Musculoskelet Disord* 2009;10:130.
47. Zhu Y, Chen RL, Miao FR, Ji L. Clinical observation on the therapeutic effect of drugs-paste separated moxibustion combined with electroacupuncture for knee osteoarthritis patients of cold-damp type. *Zhen Ci Yan Jiu* 2010;35:293-7.
48. Xu FY, Gan JH, Li WP, Yang M, Liu X. Effect of electroacupuncture on the level of IL-1beta and TNF-alpha in patients with osteoarthritis. *Zhongguo Zhen Jiu* 2009;29:529-31.
49. Manheimer E, Cheng K, Linde K, et al. Acupuncture for peripheral joint osteoarthritis. *Cochrane Database Syst Rev* 2010:CD001977.
50. Suarez-Almazor ME, Looney C, Liu Y, et al. A randomized controlled trial of acupuncture for osteoarthritis of the knee: effects of patient-provider communication. *Arthritis Care Res (Hoboken)* 2010;62:1229-36.