Traditional Chinese medicine in the management of osteoarthritis



Marc C Hochberg
University of Maryland,
Division of Rheumatology
and Clinical Immunology,
School of Medicine,
10 S Pine St, MSTF 8–34,
Baltimore, MD 21201, USA
Tel.: +1 410 706 6474;
Fax: +1 410 706 0231;
mhochber@umaryland.edu

'...some modalities of Traditional Chinese medicine are effective and should be included as part of a multidisciplinary integrative approach to management of patients with OA.'

Current recommendations for the management of patients with symptomatic osteoarthritis (OA) emphasize a multidisciplinary approach focused on the reduction of pain, functional limitation and disability [1-4]. This approach incorporates the use of nonpharmacologic modalities, including patient education, occupational and physical therapy, aerobic exercise, social support and weight loss, as well as pharmacologic therapies, including simple and opioid analgesics, NSAIDs including COX-2-selective inhibitors, and injectable agents including glucocorticoids and hyaluronan preparations. In patients whose symptoms are not adequately controlled with this approach, or who prefer not to take prescription medications because of fear of side effects, the use of traditional Chinese medicine (TCM) has been recommended as part of an integrated approach to care [5].

TCM can be defined as a range of traditional practices that originated in China and developed over a period of several thousand years [101]. Several treatment methods are considered to be part of TCM; these include herbal medicine, acupuncture (with or without moxibustion or electrical stimulation), food therapy, massage therapy, physical exercise such as T'ai Chi, mental exercise such as Feng Shui, and breathing and meditation exercise such as Qi Gong. This editorial will review the published evidence that supports the use of some TCM modalities as part of an integrative approach to the holistic management of patients with symptomatic OA.

Herbal compounds

Long and colleagues published a systematic review of randomized clinical trials (RCTs) of herbal medicines and plant extracts for OA [6]. They included 12 RCTs that reported data on

ten different compounds and used a qualitative method to summarize the evidence. The authors concluded that there was 'moderately strong evidence' for efficacy of both topical capsaicin cream and Phytodolor® (a fixed herbal formulation containing alcoholic extracts of Populus tremula, Fraxinus escelsior and Solidago virgaurea in a 3:1:1 ratio); 'promising evidence' for avocado/soybean unsaponifiables (ASU) and Devil's claw (Harpagophytum procumbens); and 'weak evidence' for Articulin-F® (an ayurvedic preparation), common stinging nettle, willow bark and Reumalex®. The authors felt there was no compelling evidence in support of ginger extract, Eazmov® (another ayurvedic preparation) or Gitadyl® (a herbal preparation containing feverfew, American aspen and milfoil).

Ernst published a separate systematic review of RCTs of ASU for OA [7]. This review included four placebo-controlled RCTs published through April 2002: three studies of 3-6 months' duration, including 587 patients with hip or knee OA, that focused on symptomatic outcomes and one study of 2 years' duration, including 163 patients with hip OA, that focused on structural outcomes. Patients randomized to ASU 300 mg once-daily had improved symptomatic outcomes and required less concomitant therapy with NSAIDs than patients randomized to placebo. However, there was no evidence of a clinically or statistically significant difference in change in joint-space width in the hip. These data suggest that ASU may be effective as an adjunctive slow-acting symptomatic drug for OA that can lead to a decrease in NSAID usage. It should be noted that these studies used the proprietary formulation of ASU marketed as Piascledine® 300 (Laboratoires Expanscience, Courbevoie, France) in Europe.

A single RCT compared Devil's claw with diacerein in the treatment of patients with hip or knee OA [8]. There was no significant difference in efficacy between the groups, although patients randomized to Devil's claw were more likely to reduce or discontinue use of concomitant NSAID therapy and were less likely to report side effects, particularly diarrhea. Another placebo-controlled RCT examined the efficacy of a



ginger extract (Eurovita Holding, Karlslunde, Denmark) in 261 patients with knee OA [9]. Patients randomized to the ginger extract had a significantly greater mean level of improvement in pain on standing and pain after walking 50 feet than those randomized to placebo; results of secondary outcome measures including the WOMACTM pain index and function- and health-related quality of life measured with the SF-12 were not significantly different between groups. Hence, there is weak evidence at best to support the efficacy of ginger extract for knee OA.

'...the use of traditional Chinese medicine (TCM) has been recommended as part of an integrated approach to care.'

Chrubasik and colleagues published a systematic review of RCTs of a preparation of rose hip and seed [10]. This review included four placebocontrolled RCTs that used a powdered extract of the seeds and husks of a Rosa canina subspecies (LitoZin®, Hyben-Vital International, Langeland, Denmark). Two studies included patients with either hip or knee OA and one each included patients with hand OA or OA at various joints; three of the studies had a crossover design, while only one was of parallel design. Based on a qualitative summary, the authors concluded that at a dose of 5 mg powder per day, there was moderate evidence of relief of joint pain after 3-4 months of therapy. However, further confirmatory evidence of efficacy is required before this compound can be recommended for use as an adjunctive therapy for OA.

Hochberg and colleagues are currently conducting a dose-escalating Phase II study of the Chinese herbal remedy Huo-Luo-Xiao-Ling Dan in patients with knee OA; this study is supported by a grant from the National Center for Complementary and Alternative Medicine. Huo-Luo-Xiao-Ling Dan contains 11 Chinese herbs with a total of 38 potential marker compounds, some of which exert anti-inflammatory activity via inhibition of COX-2 and 5-lipoxygenase [11]. A 6-week, Phase I, multiple-dose safety study was conducted in seven patients with symptomatic knee OA [12]. One patient was withdrawn because of elevated liver-function tests. There was a significant decline in knee pain during the study period, as measured with a 10-cm visual analog scale with differences from baseline reaching significance at 3 weeks. No serious adverse events occurred during this brief study.

Acupuncture

Ezzo and colleagues published a systematic review of seven RCTs of acupuncture for knee OA from 1966 to 1999 that included 393 patients [13]. Three RCTs used a sham acupuncture control group, while two each used a physical therapy and waiting-list control group; outcomes included pain in seven and physical function in six patients. Owing to the numerous types of control groups and insufficient reporting of data in individual trials, the qualitative method of best-evidence synthesis was used to summarize the results. The authors concluded that there was strong evidence that acupuncture was more effective than sham acupuncture for relief of pain; however, there was inconclusive evidence that acupuncture was more effective than sham acupuncture for function. There was inconclusive evidence that acupuncture was more effective than physical therapy for both pain and function, and there was limited evidence that acupuncture was more effective than a waiting-list control group for both pain and function. The authors suggested that future studies should define an optimal acupuncture treatment regimen and assess acupuncture in combination with other modalities.

'...traditional Chinese acupuncture is superior to sham acupuncture for treating chronic knee pain in patients with OA.'

We published the results of a three-arm RCT in 570 patients with symptomatic knee OA whose pain was not adequately controlled with analgesics and/or NSAIDs, which demonstrated that traditional Chinese acupuncture is superior to both sham acupuncture and an education control group [14]. As part of the protocol, data were collected from participants who completed the 26-week trial on healthcare utilization using the Stanford Health Assessment Questionnaire. We recently reported, based on these data, that traditional Chinese acupuncture was cost effective compared with participation in the educational program modeled after the Arthritis Self-Help Course, with an estimated cost of US\$32,000 per quality-adjusted life-year gained [15].

White and colleagues published a systematic review of RCTs of acupuncture in 2007 [16]. These authors included 13 trials involving 2362 patients; six trials were published after the review by Ezzo and colleagues (*vide supra*). The

WOMAC was used to measure pain and function in eight and seven studies, respectively. Acupuncture was significantly superior to sham acupuncture for short-term (14 weeks or less) pain relief with a weighted mean difference of 1.54 units (95% CI: 0.49-2.60); the magnitude of the difference declined but remained significant even after exclusion of the results of an outlier study. There was also a significant short-term improvement in physical function of 4.32 units (95% CI: 0.60-8.05) that remained significant after exclusion of the same outlier study. Data pooled from additional studies also showed significant improvement in long-term (26-52 weeks) pain and function with acupuncture compared with sham acupuncture. The authors concluded that traditional Chinese acupuncture is superior to sham acupuncture for treating chronic knee pain in patients with OA.

Conclusion

The available data suggest that some modalities of TCM are effective and should be included as part of a multidisciplinary integrative approach to management of patients with OA. Many herbal supplements are worthy of further study, particularly those focused on potential mechanisms of action as anti-inflammatory agents. In addition, the role of other modalities of TCM, including Qi Gong and T'ai Chi, should be evaluated further.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest
in or financial conflict with the subject matter or materials
discussed in the manuscript. This includes employment,
consultancies, honoraria, stock ownership or options, expert
testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Bibliography

- American College of Rheumatology Subcommittee on Osteoarthritis Guidelines: Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. *Arthritis Rheum.* 43, 1905–1915 (2000).
- Jordan KM, Arden NK, Doherty M et al.: EULAR Recommendations 2003: an evidence based approach to the management of knee osteoarthritis: report of a task force of the standing committee for international clinical studies including therapeutic trials (ESCISIT). Ann. Rheum. Dis. 62, 1145–1155 (2003).
- Zhang W, Doherty M, Arden N et al.:
 EULAR evidence based recommendations
 for the management of hip osteoarthritis:
 report of a task force of the EULAR
 standing committee for international
 clinical studies including therapeutics
 (ESCISIT). Ann. Rheum. Dis. 64, 669–681
 (2005)
- 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 Cart. 16, (2008) (In Press).
- Hochberg MC: Multidisciplinary integrative approach to treating knee pain in patients with osteoarthritis. *Ann. Intern. Med.* 139, 781–783 (2003).

- Long L, Soeken K, Ernst E: Herbal medicines for the treatment of osteoarthritis: a systematic review. *Rheumatol* 40, 779–793 (2001).
- Ernst E: Avocado-soybean unsaponifiables (ASU) for osteoarthritis – a systematic review. *Clin. Rheumatol.* 22, 285–288 (2003).
- Chantre P, Cappelaere A, Leblan D, Guedon D, Vandermander J, Fournie B: Efficacy and tolerance of *Harpagophytum* procumbens versus diacerein in the treatment of osteoarthritis. *Phytomed.* 7, 177–183 (2000).
- Altman RD, Marcussen KC: Effects of ginger extract on knee pain in patients with osteoarthritis. *Arthritis Rheum.* 44, 2531–2538 (2001).
- Chrubasik C, Duke RK, Chrubasik S: The evidence for clinical efficacy of rose hip and seed: a systematic review. *Phytother. Res.* 20, 1–3 (2006).
- Lee DYW, Ma ZZ, Zhang HJ et al.:
 Herbal therapies in immune mediated
 arthritis: chemistry and in vitro study of
 Chinese medicine HLXL. Presented at:
 Society for Acupuncture Research. Baltimore,
 MD, USA, 8–11 November (2007).
- Pradhan EK, Berman BM, Lee DYW, Hochberg MC, Gilpin AMK: Safety and efficacy of Huo-Luo-Xiao-Ling Dan in osteoarthritis of the knee. *Osteoarthritis Cart.* 15(Suppl. C), C221 (Abstract 408) (2007).

- Ezzo J, Hadhazy V, Birch S et al.:
 Acupuncture for osteoarthritis of the knee:
 a systematic review. Arthritis Rheum. 44,
 819–825 (2001).
- Berman BM, Lao L, Langenberg P et al.: Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: a randomized controlled trial. Ann. Intern. Med. 141, 901–910 (2004).
- Yousuf S, Frick KD, Hochberg M et al.:
 Cost effectiveness of traditional Chinese acupuncture as adjunctive therapy in osteoarthritis of the knee. Arthritis Rheum. 56(Suppl. 9), S83 (Abstract 85) (2007).
- White A, Foster NE, Cummings M, Barlas P: Acupuncture treatment for chronic knee pain: a systematic review. *Rheumatology* (Oxford) 46, 384–390 (2007).

Website

101. Traditional Chinese Medicine http://en.wikipedia.org

Affiliation

 Marc C Hochberg, MD MPH, Professor of Medicine & Head Division of Rheumatology and Clinical Immunology, University of Maryland, Division of Rheumatology and Clinical Immunology, School of Medicine, 10 S Pine St, MSTF 8-34, Baltimore, MD 21201, USA Tel.: +1 410 706 6474 Fax: +1 410 706 0231 mhochber@umaryland.edu

