

Traditional Chinese Medicine for Osteoarthritis of the Knee (TCM-OAK)

Abstract

Osteoarthritis (OA) is the most common form of arthritis and is a major cause of morbidity, limitation of activity and health care utilization, especially in the elderly. Pain and functional limitation are the primary clinical manifestations of OA. Knee OA is one of the most common joint disorders among patients with arthritis. As there are presently no curative therapies for OA of the knee, management consists of control of pain and reduction in functional limitation. However, some of the most common therapeutic approaches such as non-steroidal anti-inflammatory drugs are associated with severe side effects including gastrointestinal disturbances and cardiovascular risks. Opioids can be used to manage chronic pain, but their use is also limited by adverse effects and the risk of addiction. It has been reported that about 50% of persistent pain sufferers lack effective pain control. Traditional Chinese Medicine (TCM) is widely used to treat OA of the knee in Asian societies and is used by many in the United States. The scientific basis for its use however, is relatively sparse. Recent data suggest that inflammation plays an important role in the pathophysiology of OA with respect to both the production of pain and stiffness, and structural progression. Chinese medicine has traditionally employed mixtures of herbs in composite formulas for the treatment of various ailments. Huo-Luo-Xiao-Ling (HLXL) Dan is an ancient polyprescription that has been used for more than 400 years in the treatment of arthritis in China. We have found that an 11 herb formulation of the traditional Chinese whole herbal remedy Huo-Luo-Xiao-Ling (HLXL) Dan (活络效灵丹) has significant anti-inflammatory effects in animal models. Ten of its eleven herbs are documented to have anti-inflammatory properties, and nine to have analgesic properties.

We propose to conduct a randomized, placebo-controlled, double-blind, phase II dose-escalation clinical trial to find an optimally efficacious, safe, and tolerable dosage of HLXL extract as adjunctive treatment in 128 patients, aged 40 and over, diagnosed with OA of the knee. Twenty-eight participants will be randomized to low dose HLXL of 2,400 mg per day or placebo for 6 weeks. Then, following safety evaluation, high dose activities will be conducted. Approximately 100 participants will be randomized to high dose regimen: HLXL at 4,000 mg per day for 2 weeks, followed by HLXL 5,600 mg per day for 6 weeks, or placebo. Assessments will be carried out at baseline, 2, 4, 6 and 8 weeks for the clinically important outcomes of pain and functional limitation using valid, reliable and responsive measures – the Western Ontario McMaster (WOMAC) Osteoarthritis Index, the Patient Global Assessment (PGA), and the Medical Outcomes Study Short Form 36 (MOS SF-36), among others. We will record adverse events and symptoms and conduct blood and urine analyses, ECGs, and physical examinations. We will assess adherence with the treatment regimen via pill counts and diary, and track concomitant drug and treatment use. We will assay C reactive protein and will measure cyclo-oxygenase (COX)-1 and COX-2 activity as biological markers of inflammation and disease.