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ORIGINAL ARTICLE

Effects of Phonophoresis of Piroxicam and Ultrasound on Symptomatic Knee Osteoarthritis

Wanwadee Luksurapan, MD, Jariya Boonhong, MD

From the Department of Rehabilitation Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.

Abstract

Objective: To compare the effects of phonophoresis of piroxicam (PhP) and ultrasound therapy (UT) in patients with mild to moderate, symptomatic knee osteoarthritis (OA).

Design: A randomized, double-blind, controlled trial.

Setting: Department of rehabilitation medicine, university hospital.

Participants: Patients with knee OA (N=46; mean age ± SD, 58.91±10.50y) who had visual analog scale (VAS) scores of 50 to 92mm (mean, 71.5mm) for knee pain intensity and Kellgren-Lawrence grades of I to III were randomly allocated into 2 groups: PhP and UT (23 in each group).

Interventions: Both the PhP and UT groups were treated with an ultrasound program using the stroking technique, continuous mode, 1.0W/cm^2, 10 minutes per session, and 5 times per week for 2 weeks. Four grams of 0.5% piroxicam gel (20mg of piroxicam drug) was used in the PhP group, while the nondrug coupling gel was used in the UT group.

Main Outcome Measures: A 100-mm VAS for usual pain and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) were evaluated before and after treatment in both groups using a double-blinded procedure.

Results: The VAS and total WOMAC scores were significantly improved after treatment in both groups ($P<.001$). The PhP group showed more significant effects than the UT group, both in reducing the VAS pain score ($P=.009$) and in improving the WOMAC score, although it did not reach the level of significance ($P=.143$).

Conclusions: Our results indicated that PhP was significantly more effective than UT in reducing pain and tended to improve knee functioning in Kellgren-Lawrence grades I to III knee OA. PhP is suggested as a new, effective method for treatment of symptomatic knee OA.

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Osteoarthritis (OA) is a highly prevalent degenerative joint disease that impacts people's quality of life and puts a burden on health care costs.[1,2] OA of the knee is most common among persons 50 years and older and may cause physical disability.[3] Symptoms of knee OA include stiffness and knee pain that limits weight-bearing activities such as walking, going up and down stairs, and standing up from a chair. Symptomatic knee OA occurs in 10% of men and 13% of women 60 years and older, and is likely to increase because of the aging of the population and the obesity epidemic.[4] Treatment of knee OA is mainly directed toward reducing joint pain, as well as improving joint mobility and health-related quality of life. The international guidelines on OA recommend a combination of pharmacologic and non-pharmacologic treatment modalities in patients with knee OA.[5,6] As an alternative to oral nonsteroidal anti-inflammatory drugs (NSAIDs), the Osteoarthritis Research Society International[5] and European League Against Rheumatism[6] guidelines recommend topical NSAIDs and thermal modalities as adjunctive and alternative methods to minimize the risk of adverse events from oral NSAIDs, particularly in the elderly.

Ultrasound (US) is a deep heating agent that has been widely used to reduce pain in patients with knee OA.[7,8] US transforms electrical energy into an acoustic waveform, which is then converted into heat as it passes through tissues of varying resistances. Biological responses to US therapy (UT), through thermal and nonthermal mechanisms, include elevation of the pain threshold, alteration of neuromuscular activity leading to muscle relaxation, induction of tissue regeneration, and reduction of inflammation.[9,10]

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Phonophoresis is a therapeutic method that uses US to enhance percutaneous absorption of drugs. Phonophoresis with NSAIDs has been reported to treat pain and inflammation in many musculoskeletal conditions such as carpal tunnel syndrome, heel pain, myofascial pain, epicondylitis, muscle injury, shoulder pain, and OA.[11-17] Advantages of this method include noninvasiveness, minimal risk of adverse effects associated with systemic administration of NSAIDs, and the combined therapeutic effects of both US and NSAIDs. Despite wide usage of phonophoresis, scientific evidence to support its use is insufficient, especially in symptomatic knee OA. Previously, a randomized controlled trial[17] reported that ibuprofen phonophoresis was not superior to conventional US in treating patients with knee OA. This trial used 5% ibuprofen cream, and the treatment parameter was set at a frequency of 1MHz and 1W/cm^2 of power for 5 minutes per session. Eight of the 60 subjects in the trial had a severe grading of OA (Kellgren-Lawrence grade IV). A review article[18] summarized that treatment parameters to conduct phonophoresis, including the duration of the procedure and the forms of drugs, are factors influencing the efficacy of this technique. In our setting, the duration of UT was normally set at 10 minutes per session, because a duration of 5 minutes per session may not reach a therapeutic dose. A gel-type topical drug was the best composition when compared with cream or emulsion regarding the capacity of US conduction.[19] Following international guidelines, conservative management is appropriate for knee OA of mild to moderate severity; however, severe knee OA (Kellgren-Lawrence grade IV) may not respond to the conservative treatment. Currently, no other study has examined phonophoresis in knee OA. A study that establishes the superiority of phonophoresis to conventional US would be valuable because it would lead to the development of more effective modalities with minimal side effects and lower costs.

Piroxicam gel was shown to be safe and efficacious for treatment in musculoskeletal pain.[20] It is available in Thailand and affordable. Furthermore, the odorless and transparent blue gel is similar to standard gel and has the perfect quality of blinding participants and therapists from awareness of which gel they received.

We conducted this randomized controlled trial to compare the effects of phonophoresis of piroxicam (PhP) with UT in reducing pain and improving the function of patients with symptomatic knee pain caused by mild to moderate OA.

Methods

Participants

The study's protocol was approved by the institutional review board of the Faculty of Medicine, Chulalongkorn University. All enrolled participants provided written informed consent. Data collection and participants follow-up took place at the Department of Rehabilitation Medicine, King Chulalongkorn Memorial Hospital, Bangkok, from October 2010 to September 2011.

Patients enrolled in the study consisted of 45 women and 1 man, between the ages of 26 and 78 years (mean age ± SD, 58.91±10.50y), who fulfilled the American College of Rheumatology criteria for OA of the knee.[21] Their Kellgren-Lawrence[22] scores were grades I to III, and their visual analog scale (VAS) scores for pain were ≥50mm. Patients were excluded from the study if they had knee pain attributable to causes other than OA (eg, tendonitis, bursitis), other chronic systemic inflammatory diseases, a history of allergy to piroxicam, a recent history of knee injury or surgery, or used medication that might potentially confound study assessments (eg, NSAIDs, corticosteroids, tramadol hydrochloride).

List of abbreviations:

ANCOVA	analysis of covariance
CI	confidence interval
NSAIDs	nonsteroidal anti-inflammatory drugs
OA	osteoarthritis
PhP	phonophoresis of piroxicam
US	ultrasound
UT	ultrasound therapy
VAS	visual analog scale
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

Study design and randomization

This study was a randomized, double-blind, controlled trial. After screening, patients who met the eligibility criteria were randomly allocated to the treatment groups of PhP or UT. The block of 4 randomization schedules was computer-generated and sealed in opaque, tamperproof, and numbered envelopes. The patients did not know which study group they were in. We took several measures to ensure blinding in both the study personnel and the patients. With the exception of an assigned research assistant, none of the personnel knew the randomized sequence. The research assistant would record the name, number, and study group of the patients, and prepare the study gel in a concealed package following the randomized list.

Treatment procedures

Phonophoresis of piroxicam

The study gel was prepared by mixing the 0.5% piroxicam gel[a] with a standard coupling agent at a ratio of 4:11 by volume. The 15cm^3 of mixed gel (about 20mg of piroxicam drug) was prepared in a concealed container and sent to the physical therapists by the assistant for each subject in every session. Its color and odor were quite similar to the coupling agent routinely used for UT. During the treatment, staff members were asked not to guess or talk about the treatment gel to participants. The continuous mode (1.0W/cm^2 power and 1MHz frequency of US wave) was conducted with the stroking technique, using the Sonopuls 491.[b] Patients received a total of 10 sessions (5 times a week for 2 weeks, excluding weekends), with each session lasting 10 minutes. Before starting the treatment, the therapist would thoroughly clean the subjects' skin with alcohol.

Ultrasound therapy

This procedure was exactly like PhP but without the use of piroxicam gel. The nondrug, standard coupling gel was prepared using an identical container, gel volume, and other processes as for PhP. The purpose of the UT group was to identify the effect of UT alone and to serve as the control group.

Patients in both groups received paracetamol (500-mg tablets) as a rescue medication, 1 or 2 tablets every 6 hours to a maximum of 8 tablets when their pain was intolerable. They were also asked to record the number of tablets taken and write the date of use on a given record card. Additional medications such as oral NSAIDs, opioids, muscle relaxants, or topical drugs were not allowed. The