**ARAŞTIRMA MAKALESİ**

**Dilek Durmuş**[1]
**Mustafa Unal**[2]

[1]MD, Professor, Department of Physical Medicine and Rehabilitation, Medical Faculty, Ondokuz Mayis University, Samsun, Turkey
[2]MD, Assistant Professor, Department of Family Medicine, Ondokuz Mayis University, Samsun, Turkey

***Yazışma Adresi:***
*Mustafa Unal,*
*MD, Assistant Professor, Department of Family Medicine, Ondokuz Mayis University, Samsun, Turkey*
*Telephone: 00903623121919-2744*
*Fax: 00903624576041*
*E-mail: drmustafa2@gmail.com*

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konuralptipdergi@duzce.edu.tr
konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

# Diz Osteoartritinde Kapsaisin Fonoforezin Etkisi ve Birinci Basamakta Erken Kullanılabilirliği: Randomize Kontrollü Bir Çalısma

**ÖZET**

**Amaç**: Bu çalışmanın amacı Kapsaisin fonoforezis ve kapsaisin jelin diz osteoartritinin tedavisinde ağrı, engellilik, fonsiyonalite, uyku kalitesi ve depresyon üzerine etkilerini değerlendirmektir.

**Gereç ve Yöntem**: Yetmiş üç hasta 3 gruba ayrıldı. Tüm gruplara egsersiz tedavisi uygulandı. Egsersize ek olarak birinci gruba (n = 24) kapsaisin fonoforezis, ikinci guruba (n = 24) kapsaisin jel uygulandı. Tedaviler haftada 3 gün, 6 hafta uygulandı. Hastalar ağrı için görsel analog skala, engellilik için Western Ontario ve McMaster Universite Osteoartrit Indeksi, fonksiyon için 50 m yürüme zamanı, depresyon için Beck Depresyon Skalası ve uyku kalitesi için Pittsburgh Uyku Kalite indeksi ile değerlendirildi. Değerlendirilmeler tedavi sonrası ve 1 aylık izlemde yapıldı.

**Bulgular**: Tüm guruplar tüm parametrelerde iyileşme gösterdi. Ağrı skor sonuçları grup 1 de daha iyi idi. Bu iyilik bir ay izleminde hala devam ediyordu. Grup 1 ve 2 arasında engellilik, fonksiyon, depresyon ve uyku kalitesi açısından fark bulunmadı.

**Sonuç**: Kapsaisin fonoferezis ağrıyı azaltmada egsersiz ve kapsaicin jele göre daha etkilidir. Kapsaisin jelin haftada sadece 3 defa kullanılmasına rağmen fonksiyon, engellilik ve uyku kalitesi üzerine capsaisin fonoferesiz kadar etkili olduğu ve aynı zamanda egsersizin uyku kaliesi ve fonksiyon üzerine etkisini artırdığı gösterildi. Bu sonuç özellikle birinci basamakta kapsaicin jel kullanımını teşvik etmektedir.

**Anahtar Kelimeler**: Diz osteoartriti, fonoforezis, kapsaisin

# The effect of capsaicin phonophoresis in knee osteoarthritis and can it be utilized early in primary care? : A randomized-controlled trial

**ABSTRACT**

**Aim:** The aim of this study is to evaluate the effect of capsaicin phonophoresis (PP) and capsaicin gel in the treatment of knee osteoarthritis (OA) on scores of pain, disability, functionality, sleep quality and depression.

**Method:** Seventy-three patients divided into 3 groups. All groups receieved exercise therapy. Addition to exercise, group 1 (n = 24) received capsaicin PP, Group 2 (n = 24) capsaicin gel. Therapies applied 3 days a week, for 6 weeks. Patients were evaluated with visual analogue scale (VAS) for pain, Western Ontario and McMaster University Osteoarthritis Index for disability, 50-m walking time for functionality, Beck Depression Inventory Scores for depression and Pittsburgh Sleep Quality Index for sleep quality. Evaluations are done after the therapy, and at 1-month follow up.

**Results:** All groups improved significantly in all parameters. Pain scores after treatment were better in group 1. Regarding pain scores at follow up it was still effective. Regarding disability, functionality, depression and sleep quality no difference found between group 1 and 2.

**Conclusion:** Capsaicin Phonophoresis is more effective in reducing pain compared to exercise and capsaicin gel. Capsaicin gell was as effective as Capsaicin Phonophoresis on functionality, disability and sleep quality and also more effective than exercise alone on functionality and sleep despite using 3 times a week. This result encourages capsicin gel usage in the treatment of knee osteoarthritis especially in primary care.

**Key words:** Knee osteoarthritis, phonophoresis, capsaicin

## INTRODUCTION

Osteoarthritis (OA) is one of the most common rheumatologic conditions and dominates primary care and physical therapy and rehabilitation (PTR) visits of the aged population. OA is chronic disease characterized by the focal deterioration and abrasion of articular cartilage. OA is major cause of pain, physical disability, and muscle weakness in mainly aged population leading to physical and psychological problems, insomnia, and depression (1,2).

The objectives of management of knee OA are to relieve pain and to maintain or improve functionality. Family physicians (FP) treat OA in stepwise program (1). The first step is exercise and the last step is surgery. Before recommending surgery a FP makes sure all treatment options utlilised optimally. PTR clinics use exercise, sound waves and topical agents more often. Early referral to PTR for structured exercise and specialised treatment would be more beneficial (1). Clinical guidelines followed in PTR for managing knee OA recommend a combination of nonpharmacologic (i.e. education, exercise, lifestyle changes and physical therapy) and pharmacologic (i.e. paracetamol, nonsteroidal antiinflammatory drugs (NSAlDs), and topical agents including capsaicin gel) treatments (3-6). Complexity and the management difficulty of OA necessaties collaboration of different disciplines in medicine. Primary care physician is not only expected to diagnose and treat OA, also refer to specialised treatment and surgery. This study gave us insight about different treatment options used in PTR clinics.

Sound waves although not commonly used in primary care, are used in OA and may be administered in either a continuous or a pulsed mode (7). Pulsed US produces non-thermal effects and is used to aid in the reduction of inflammation, whereas continuous US generates thermal effects (8,9). Phonophoresis (PP) uses high-frequency sound waves to deliver therapeutic medications of mainly topical analgesics or steroids, through the skin into the deeper tissues. Therapeutic effects of topical drugs depend on different factors such as amount and drug penetration depth of the skin (10,11). PP and ultrasound (US) therapy are well tolerated, noninvasive and painless methods used in musculoskeletal disorders 10,11

Primary goals of rehabilitation of musculoskeletal problems are to decrease symptoms, optimize daily functionality and reduce disability (12).

The PP therapy is used predominantly in musculoskeletal disorders such as myofascial pain syndrome, knee OA, carpal tunnel syndrome, epicondylitis, impingement, and tenosynovitis (10, 13-18). Despite extensive clinical trials of PP, questions remain regarding treatment effectiveness (10, 13-21). There are no FP guidelines recommending PP and capsaicin in the treatment of knee OA. Additionally, in the literature there is no study evaluating the efficacy of capsaicin pp in knee OA following treatment and after 1 month follow up. Aim of this study was to demonstrate a succesfull partnership between FM and PTR in determining and comparing the effects of capsaicin PP, topical capsaicin gel in addition to exercise therapies on pain, disability, functional performance, sleep quality, and depression in patients with knee OA.

## METHODS

### Study design

This prospective randomized-controlled clinical trial was conducted at the Department of Physical Medicine and Rehabilitation, Medical Faculty of Ondokuz Mayis University, Samsun, Turkey. The patients who had been diagnosed as knee OA according to American College of Rheumatology (ACR) criteria were enrolled in the study. Standing anteroposterior and lateral radiographs of both knees were obtained, and the severity of OA in the tibiofemoral compartment was graded according to the criteria of Kellgren-Lawrence. Exclusion criteria were serious medical conditions that limits exercise, neuromuscular or dermatologic disease that involves the lower extremities, any exercise program that may increase muscle strength in the last 6 months, existence of implanted cardiac pacemaker or defibrillator, inflammatory arthropathy, contracture, story of trauma within the previous 6 months, intraarticular injection of hyaluronic acid, steroids or US therapy in the last 6 months, and grade 4 OA.

In order to achieve statistical power of 0.98, and $P < 0.05$, the minimum number of subjects per group was estimated 23 for WOMAC pain (Western Ontario and McMaster University Osteoarthritis Index scores).

The demographic data included age, body mass index (BMI) (kg/m2), educational level, and duration of symptoms (years). The occupations of subjects were housewives, employee, or retired. The patients were informed about the purpose of the study and gave their consent. The study protocol was approved by the local ethics committee.

### Randomization

The patients (n=75) were randomized into three groups. Randomization was allocated by numbered envelopes method. Group 1 received PP with capsaicin and exercise therapy. Group 2 received topical agents as capsaicin gel and exercise therapy. Group 3 only received exercise therapy. All patients were evaluated in the out-patient settings. All of the programs were performed 3 days a week, for 6 weeks. Patients were evaluated before and after the treatment (2 patients failed to attend), and at 1-month follow-up. NSAlDs or analgesic drugs were not used during the study and the patients are cautioned not to use them.

### Phonophoresis therapy

Ultrasound device (Enraf Nonius Sonoplus 434) was used. Topical gel of capsaicin (10 % capsicum oleorisin 0.20 %) was applied circularly with a thickness of 2–3 mm then ultrasound with a 5-cm-diameter applicator was used over the both knee region with 1 MHz frequency and 1.5 Wt/cm2 power. The treatment duration was 10 min(16).

### Topical capsaicin gel therapy

Topical 10 % capsicum oleorisin 0.20 % gel is applied to the knee region.

**Exercise therapy**

The subjects in all 3 groups were treated with a group-exercise program composed of 45 min cervical, thoracic, lumbar, abdominal, and knee exercises with a warm-up and cool-down period of 10 min stretching exercises 3 days a week under the supervision of the physiatrist. All patients came to the outpatient department for exercise treatments. Knee exercise program included isotonic, isometric, active range-of-motion, flexibility and stretching. Additional exercises were; 1. Motion, flexibility, and back strengthening exercises of the thoracic, and lumbar spine; stretching of the erector spine muscle, hamstring muscles, pelvic muscles, and abdominal muscles (pelvic tilt, knee to chest, lower abdominal exercises, cat and camel, back extension exercises.) 2. Special exercises to improve the mobility of the spine and hip joints, activate the stabilize muscles of the spine, and increase flexibility of the lower limb muscles. 3. Functional exercises to improve postural control, dynamic body balance, and coordination. 4. Progressive relaxation exercises to normalize muscle tension.

**Clinical assessments**

Pain, disability, functional performance, sleep quality, and depression were assessed before the treatment, after the sixth week of the therapy, and at 1-month follow up.

**Pain and disability**

Patients were asked to grade the intensity of the pain at resting and during activity on a 10-cm visual analogue scale (VAS) as '0' is no pain and '10' is most severe pain (22). Outcome measures for pain evaluated with WOMAC pain score (22). Disability was assessed with WOMAC physical function score (22). Functional performance was objectively assessed with the timing of patients walking as fast as they could for 50 m (22).

**Sleep quality**

The Pittsburgh Sleep Quality Index (PSQI) was used for the assessment of sleep quality. The PSQI is a questionnaire consisting of 19 items which are coded on a 4-point scale (0-3) in 7 subcategories, including sleep duration, sleep disturbances, sleep latency, daytime dysfunction, sleep efficiency, sleep quality and medication usage. The sum of all sub scores represents the total sleep quality score, ranging between 0–21, with higher scores representing lower sleep quality. Respondents are asked to rate their sleep for the last month. The validity and reliability of the Turkish form of PSQI was performed by Agargun et al. (23).

**Depression**

Depression was assessed with Beck Depression Inventory (BDI). BDI is a 21-item test presented in multiple-choice format aims to measure presence and degree of depression. Responses are made on a four-point scale from 0 to 3, with 3 representing the most severe symptoms (24).

**Statistical analysis**

Statistical analyses were performed with SPSS 15.0 for windows. Descriptive data were presented as mean ± standard deviation (SD) and minimum–maximum (median). The Shapiro–Wilk test was used to analyze normal distribution assumption of the quantitative outcomes. Baseline, after treatment, and follow up clinical properties of the groups were compared using the nonparametric Kruskal–Wallis and also Mann-Whitney U tests. Wilcoxon's signed rank test or paired t test was used for in-group changes. The sociodemographical characteristics were evaluated by Chi-square test. P values less than 0.05 were considered statistically significant.

**RESULTS**

Seventy-five (75) female patients were volunteered in this study. Seventy-three (73) completed the study (one in the PP group and one in the capsaicin gel group failed to attend to the 6th week assessment) (Figure 1-Flow chart-Overall plan of the study).

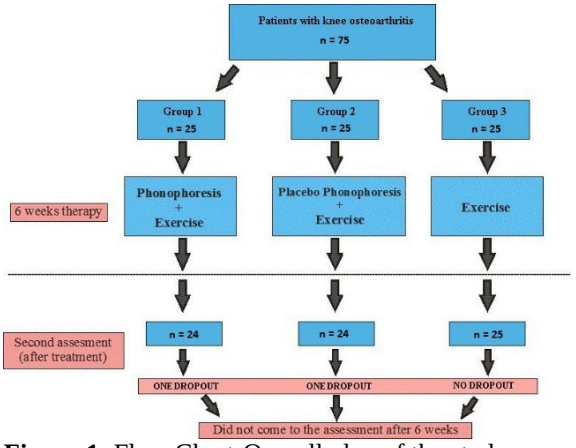


**Figure 1**: Flow Chart-Overall plan of the study

Demographic properties of the patients are shown in Table 1. There was no statistically significant difference regarding the age, body mass index, duration of symptoms, and employment status among the groups (P > 0.05).

As far as pain, disability, functional performance, sleep quality, and depression scores were concerned no differences were present between groups before treatment (P > 0.05) (table 3).

**Pain and disability**

Pain and disability scores improved significantly in all groups (Table 2). VAS and WOMAC Pain scores after treatment were better in group 1. Regarding Vas scores at follow up group 1 was better than group 2 but there was no difference between groups 1 and 3. Regarding WOMAC pain scores at follow up there were no difference between groups. Regarding disability, no difference found between group 1 and 2 and group 1 was better than group 3 after treatments. Detailed results are presented in table 3 and 4.

**Functional performance**

50 m walking time scores improved significantly in all three groups when compared with their initial status (P < 0.05; Table 2). There were no differences between groups 1 and 2. Group 1 and 2 were better than group 3. All results can be seen in table 3 and 4.

**Sleep quality and Depression**

Sleep quality scores improved significantly in all three groups when compared with their initial status (P < 0.05; Table 2). There were no differences between groups 1 and 2. Group 1 and 2 were better than group 3. Regarding depression scores there were no differences between groups in both after treatment and follow up. All results can be seen in table 3 and 4.

**Table 1:** Clinical and demographic features of the patients

| | **Group 1 (n=24)** | **Group 2 (n=24)** | **Group 3 (n=25)** | **p** |
|---|---|---|---|---|
| **Age (year) Median (Min-Max)** | 56.5(49-65) | 57.0(42-70) | 56.0(48-70) | 0.538 |
| **BMI (kg/m$^2$) Median (Min-Max)** | 27(20-32) | 27(21-35) | 27(23-34) | 0.343 |
| **Duration of symptoms (year) Median (Min-Max)** | 4(1-13) | 6(1-15) | 5(1-10) | 0.142 |
| **Job n (%)** | | | | 0.323 |
| **Housewife** | 5 (20.9) | 8 (33.4) | 9 (36.0) | |
| **Retired** | 16 (66.6) | 13 (54.1) | 14 (56.0) | |
| **Officer** | 3 (12.5) | 3 (12.5) | 2 (8.0) | |
| **Education n (%)** | | | | 0.233 |
| **Primary education** | 2 (8.3) | 5 (20.9) | 5 (20.0) | |
| **Secondary education** | 6 (25.0) | 7 (29.1) | 9 (36.0) | |
| **College** | 16 (66.7) | 12 (50.0) | 11 (44.0) | |
| **Knee grade n (%)** | | | | 0.750 |
| **I** | 10 (41.7) | 8 (33.3) | 9(36.0) | |
| **II** | 9 (37.5) | 11(45.8) | 10(40.0) | |
| **III** | 5 (20.8) | 5(20.9) | 6 (24.0) | |

P<0.05 significant
**The severity of OA was graded according to the criteria of Kellgren-Lawrence**

**Table 2:** Baseline and after treatment results of clinical parameters

| | **Group 1 (n=24)** | | | **Group 2 (n=24)** | | | **Group 3 (n=25)** | | |
|---|---|---|---|---|---|---|---|---|---|
| | BT Mean±SD Median(min-max) | AT Mean±SD Median(min-max) | p | BT Mean±SD Median(min-max) | AT Mean±SD Median(min-max) | p | BT Mean±SD Median(min-max) | AT Mean±SD Median(min-max) | p |
| **VAS pain** | 4.77±1.76 5(2-8) | 1.00±0.90 1(0-3) | **0.001** | 4.16±1.54 3.5(2-8) | 1.61±0.84 1.5 (0-3) | **0.001** | 5.36±2.03 5(2-8) | 3.10±1.94 3(0-7) | **0.001** |
| **WOMAC pain** | 5.55±2.77 5(2-13) | 1.16±1.09 1(0-4) | **0.001** | 5.50±2.91 4.5 (1-11) | 2.50±1.75 2(0-6) | **0.001** | 7.21±3.72 7(1-15) | 4.68±3.05 4 (0-11) | **0.001** |
| **WOMAC disability** | 16.72±10.45 15.5(2-40) | 4.61±4.40 3(0-28) | **0.001** | 17.22±12.12 14(1-45) | 8.55±6.68 6.5 (0-22) | **0.001** | 24.10±11.60 27 (5-45) | 17.63±10.42 15 (3-42) | **0.001** |
| **50 m walking time (seconds)** | 55.27±4.18 54.5 (49-65) | 48.33±2.52 48 (45-55) | **0.001** | 56.77±3.71 56 (49-63) | 50.66±2.67 50 (46-56) | **0.001** | 56.68±4.74 57 (48-65) | 53.31±3.81 54 (47-60) | **0.001** |
| **BDI score** | 7.83±5.52 7.5 (2-19) | 3.38±2.68 3(0-10) | **0.001** | 9.94±5.95 9 (1-22) | 3.94±3.36 3.5 (0-12) | **0.001** | 10.63±5.65 10 (1-23) | 6.26±3.61 5 (1-6) | **0.001** |
| **PSQI Total** | 8.72±4.34 9 (0-17) | 3.00±1.94 3(0-6) | **0.001** | 8.66±4.69 8.5(1-22) | 3.66±2.40 3.5 (0-10) | **0.001** | 7.68±3.52 8 (1-15) | 5.89±2.78 6 (1-12) | **0.001** |

**BT** Before treatment
**AT** After treatment
**VAS pain** visual analog scale pain
**WOMAC pain** Western Ontario McMaster osteoarthritis index pain
**BDI** beck depression Index
**PSQI** Pitsburg sleep quality Index
**Mean±SD** Mean±Standart Deviation
**P<0.05 Significant**

**Table 3.** Evaluations of clinical parameters between the groups for change scores after treatment-before treatment and follow up

| Characteristics | | Group 1 (n=24) | | Group 2 (n=24) | | Group 3 (n=25) | | p |
|---|---|---|---|---|---|---|---|---|
| | | Mean ± SD | Med (min;max) | Mean ± SD | Med (min;max) | Mean ± SD | Med (min;max) | |
| **VAS pain** | BT | 4.77±1.76 | 5(2-8) | 4.16±1.54 | 3.5(2-8) | 5.36±2.03 | 5(2-8) | 0.169 |
| | AT-BT | -3.77± 1.26 | -4 (-6; -2) | -2.11 ± 1.09 | -2.5 (-5; -1) | -2.26 ± 0.65 | -2 (-3; -1) | **0.001** |
| | F-BT | -1.50 ± 0.61 | -1 (-3 ; -1) | -0.77 ± 0.54 | -1 (-2 ; 0) | -1.21 ± 0.53 | -1 (-2 ; 0) | **0.030** |
| **WOMAC pain** | BT | 5.55±2.77 | 5(2-13) | 5.50±2.91 | 4.5 (1-11) | 7.21 ± 3.72 | 7(1-15) | 0.235 |
| | AT-BT | -4.44 ± 1.94 | -4 (-9; -2) | -3.00 ± 1.45 | -3 (-5; -1) | -2.52 ± 1.12 | -2 (-4; -1) | **0.005** |
| | F-BT | -2.00 ± 1.28 | -2 (-4 ; 0) | -1.27 ± 0.82 | -1 (-3; 0) | -1.89 ± 1.41 | -2 (-6; 0) | 0.168 |
| **WOMAC disability** | BT | 16.72±10.45 | 15(2-40) | 17.22±12.12 | 14(1-45) | 24.10±11.60 | 27 (5-45) | 0.110 |
| | AT-BT | -12.11 ± 4.47 | -12 (-31; -2) | -8.44 ± 5.65 | -7.5 (-23; -1) | -6.47 ± 4.07 | -5 (-17; -2) | **0.043** |
| | F-BT | -4.00 ± 2.72 | -3 (-8 ; 0) | -3.33 ± 2.42 | -3 (-8 ; 0) | -4.94 ± 3.20 | -4 (-12 ; -1) | 0.284 |
| **50 m walking time (seconds)** | BT | 55.27±4.18 | 54.5 (49-65) | 56.77±3.71 | 56 (49-63) | 56.68±4.74 | 57 (48-65) | 0.336 |
| | AT-BT | -6.94 ± 1.92 | -7 (-10; -3) | -6.11 ± 1.71 | -6 (-10; -3) | -3.36 ± 1.38 | -3 (-6; 0) | **0.001** |
| | F-BT | -3.72 ± 1.90 | -3.5 (-8 ; -1) | -3.88 ± 1.45 | -4 (-7 ; -1) | -2.42 ± 1.70 | -3 (-5 ; 0) | **0.038** |
| **BDI score** | BT | 7.83±5.52 | 7.5 (2-19) | 9.94±5.95 | 9 (1-22) | 10.63±5.65 | 10 (1-23) | 0.286 |
| | AT-BT | -4.44 ± 3.43 | -4 (-14; 0) | -6.00 ± 2.97 | -6 (-12; -1) | -4.36 ± 2.43 | -4 (-9; 0) | 0.163 |
| | F-BT | -3.00 ± 2.93 | -2 (-12 ; 0) | -3.33 ± 2.89 | -3 (-10 ; 0) | -3.00 ± 1.85 | -3 (-7 ; 0) | 0.840 |
| **PSQI Total** | BT | 8.72±4.34 | 9 (0-17) | 8.66±4.69 | 8.5(1-22) | 7.68±3.52 | 8 (1-15) | 0.735 |
| | AT-BT | -5.72± 3.04 | -5 (-11; 0) | -5.00 ± 2.52 | -5 (-12; -1) | -1.78 ± 0.91 | -2 (-3; 0) | **0.001** |
| | F-BT | -4.11 ± 2.27 | -4 (-8 ; 0) | -3.55 ± 2.30 | -3 (-10 ; -1) | -1.15 ± 0.83 | -1 (-2 ; 0) | **0.001** |

**BT** Before treatment
**AT** After treatment
**F** Follow up
**VAS pain** visual analog scale pain
**WOMAC pain** Western Ontario McMaster osteoarthritis index pain
**PSQI** Pitsburg sleep quality Index
**Mean±SD** Mean±Standart Deviation
**P<0.05 Significant**
**P= Differences between the groups**

**Table 4.** Differences between the groups for change scores after treatment-before treatment and follow up

| | | Group 1(n=24) Mean±SD | Group2(n=24) Mean±SD | p* | Group3(n=25) Mean±SD | p** | p*** |
|---|---|---|---|---|---|---|---|
| **VAS pain (cm)** | AT-BT | -3.77± 1.26 | -2.11 ± 1.09 | **0.002** | -2.26 ± 0.65 | **0.001** | 0.480 |
| | F-BT | -1.50 ± 0.61 | -0.77 ± 0.54 | **0.004** | -1.21 ± 0.53 | 0.245 | 0.061 |
| **WOMAC pain** | AT-BT | -4.44 ± 1.94 | -3.00 ± 1.45 | **0.029** | -2.52 ± 1.12 | **0.001** | 0.343 |
| | F-BT | -2.00 ± 1.28 | -1.27 ± 0.82 | 0.097 | -1.89 ± 1.41 | 0.730 | 0.150 |
| **WOMAC disability** | AT-BT | -12.11 ± 4.47 | -8.44 ± 5.65 | 0.192 | -6.47 ± 4.07 | **0.014** | 0.210 |
| | F-BT | -4.00 ± 2.72 | -3.33 ± 2.42 | 0.462 | -4.94 ± 3.20 | 0.374 | 0.134 |
| **50 m walking time (seconds)** | AT-BT | -6.94 ± 1.92 | -6.11 ± 1.71 | 0.214 | -3.36 ± 1.38 | **0.001** | **0.001** |
| | F-BT | -3.72 ± 1.90 | -3.88 ± 1.45 | 0.606 | -2.42 ± 1.70 | 0.070 | **0.016** |
| **PSQI Total** | AT-BT | -5.72± 3.04 | -5.00 ± 2.52 | 0.521 | -1.78 ± 0.91 | **0.001** | **0.001** |
| | F-BT | -4.11 ± 2.27 | -3.55 ± 2.30 | 0.372 | -1.15 ± 0.83 | **0.001** | **0.001** |

**BT** Before treatment
**AT** After treatment
**F** Follow up
**VAS pain** visual analog scale pain
**WOMAC pain** Western Ontario McMaster osteoarthritis index pain
**PSQI** Pitsburg sleep quality Index
**Mean±SD** Mean±Standart Deviation
**P<0.05 Significant**
*** Differences between group 1 and 2, ** Differences between group 1 and 3,**
***** Differences between group 2 and 3**

**DISCUSSION**

Osteoarthritis is a common degenerative joint disease that impacts quality of life. It is an age-related condition, occurring more frequently in women (25). The aim of the treatment in the knee OA is to decrease pain, increase mobility, prevent disability, and improve sleep quality and physical functions. To achieve these aims, various treatment programs are suggested. Medications, physical therapy, superficial-deep heat applications, PP, and exercises are the therapies often administered (3-6,22). The effects of the PP on knee OA were studied in a few randomized-controlled studies and there is no consensus on the efficacy of the treatment (13, 18-20).

This study was planned as a randomized single-blind, controlled study. We investigated the efficacy of capsaicin PP in comparison to topical capsaicin gel and exercise on pain, disability, functional performance, sleep quality, and depression in knee OA. While all of the groups showed significant improvements in all parameters PP capsaicin group showed better improvement regarding pain. Family physicians could specifically recommend PP capsaicin therapy in knee OA when pain is the primary symptoms.

Therapeutic US is a well-established method turning mechanical energy to a form of sound waves for the purpose of heating deep tissues thus, reducing edema, relieving pain, increasing range of motion and accelerating tissue repair in many musculoskeletal diseases (26,27). PP is a therapeutic method used with US (10). The cell permeability, transdermal migration by local vasodilatation (10) are increased thus percutaneous absorption of intended drugs are enhanced (28,29).

PP with NSAIDs has been reported to treat pain and inflammation in many musculoskeletal conditions such as carpal tunnel syndrome, myofascial pain, neck pain, impingement, muscle injury, and knee OA (10, 13-18). 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.

Different topical drugs such as local anesthetics, anti-inflammatory drugs (steroidal and nonsteroidal medications) are used in PP (19,20,30-32). There are limited randomized controlled studies regarding the efficacy of PP on knee OA in the literature. Kozanoglu et al. (13) compared the effectiveness of 5 % ibuprofen PP and US treatment in the patients with knee OA and they found no difference between them. Luksurapan et al (20). compared the effectiveness of piroxicam PP and US therapy in patients with mild to moderate, knee OA and they reported that PP was significantly more effective than US in reducing pain and improving knee functions. Boyacı et al (19). compared the effectiveness of ketoprofen PP, short-wave diathermy, and US therapy in knee OA with VAS, WOMAC and 15-m walking time. Although all methods were effective, they found no difference between them. We used capsaicin PP and as far as we know capsaicin is not being used in knee OA before.

Our study is not designed to compare the effectiveness of capsaicin PP and US as opposed to mentioned studies. We made comparisons between topical capsaicin, exercise and PP capsaicin. The improvements in pain scores with capsaicin PP were significantly better than other methods. After 6 weeks therapy period patients had one month without any treatment and evaluated again. In this evaluation capsaicin PP group's VAS scores showed that capsaicin PP was still effective. This effect was statistically significant but WOMAC pain scores were not statistically significant although they were still better. On disability capsaicin PP was better than exercise.

Capsaicin, binds to nociceptors in the skin, causing an initial excitation of the neurons and a period of enhanced sensitivity. This is usually perceived as itching, pricking, or burning, with cutaneous vasodilatation, and is thought to be due to selective stimulation of afferent C fibres and release of substance P (33). A metaanalysis in Cochrane library states Capsaicin Gel Formulations ranged from 0.025 % - 0.075% 3-4 times a day for 4- 12 weeks is used in trials. It is well tolerated and moderately effective with only significant side effects of burning sensation (34-36). Our study was designed to research the efficacy of Capsaicin PP. To establish inter group's standardization Capsaicin PP, topical capsaicin and exercise were applied 3 times a week. Similar to previous studies we found topical capsaicin gel is effective. Topical Capsaicin on functionality, disability and sleep quality in knee OA was as effective as PP capsaicin even though it is used only 3 times a week and topical capsaicin was more effective than exercise alone in functionality and sleep. This suggests topical capsaicin may be used in primary care as a first choice agent.

Regular exercise can improve pain control, proprioception, strength, instability, and endurance, all of which improve functional independence in knee OA (37-39). Similarly, we found an improvement in all clinical parameters in exercise group. Exercise therapies are integral part of family medicine and all FPs should be involved tailoring exercises in different clinical conditions.

Our study has some limitation. First, all patients were women (men were offered to take part but they declined due to work). Second, the study sample size could have been larger. Third, usage of capsaicin gel 3 times a week due to standardization of the groups could be counted as a limitation as recommended usage in studies is 3, 4 times a day. This yielded surprising results as capsaicin was stil effective.

In conclusion we determined that capsaicin PP was significantly more effective than capsaicin gel for reducing pain in knee OA even after a month. Capsaicin PP also increased the efficacy of exercise in reducing the pain, improving functionality and sleep quality. Therefore, we recommend capsaicin PP in the treatment of knee OA together with exercise therapy.

Topical Capsaicin on functionality, disability and sleep quality in knee OA was as effective as PP capsaicin. Additionally, topical capsaicin was more effective than exercise alone in functionality and sleep. Utilising nonpharmacological therapies and local agents more efficiently may decrease number of systemic drugs and side effects. Older patients usually have multiple health problems that requires multi-drug treatment. In our view, usage of capsaicin 3 times a week might have increased patient compliance and decreased side effects such as burning feelings. For these reason patients who have compliance problems for any reason may use and benefit from irregular use of local capsaicin. Close study of family physicians and PTR will benefit patient and increase the job satisfaction of the doctors.

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**REFERENCES**


1. Sinusas K. Osteoarthritis: Diagnosis and Treatment. Am Fam Physician. 2012: 1; 85:49-56
2. Pelletier JP, Martel-Pelletier J, Abramson SB. Osteoarthritis, an inflammatory disease: potential implication for the selection of new therapeutic targets. Arthritis Rheum. 2001: 44:1237– 1247
3. Petrella RJ. Is exercise effective treatment of osteoarthritis of the knee? Br J Sports Med. 2000; 34:326–331
4. Baker K, McAlindon T. Exercise for knee osteoarthritis. Curr Opin Rheumatol. 2000; 12:456–463
5. 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
6. Zhang W, Doherty M. EULAR recommendations for knee and hip osteoarthritis: a critique of the methodology. Br J Sports Med. 2006; 40:664-9
7. Wright A, Sluka KA. Nonpharmacological Treatments for Musculoskeletal Pain. Clin J Pain. 2001; 17: 33–46
8. Rutjes AW, Nu¨ esch E, Sterchi R, et al. Therapeutic ultrasound for osteoarthritis of the knee or hip (Review). Cochrane Database Syst Rev 20: CD003132, 2010
9. Johns LD. Nonthermal effects of therapeutic ultrasound: the frequency resonance hypothesis. J Athl Train.2002; 37: 293–9
10. Ay S, Doğan SK, Evcik D, et al. Comparison the efficacy of phonophoresis and ultrasound therapy in myofascial pain syndrome. Rheumatol Int. 2011; 31:1203-8
11. Rand SE, Goerlich C, Marchand K, et al. The physical therapy prescription. Am Fam Physician.2007;1;76:1661-6
12. Koldas Dogan S, Sonel Tur B, Kurtais Y, et al. Comparison of three different approaches in the treatment of chronic low back pain. Clin Rheumatol. 2008; 27:873–81
13. Kozanoglu E, Basaran S, Guzel R, et al. Short term efficacy of ibuprofen phonophoresis versus continuous ultrasound therapy in knee osteoarthritis. Swiss Med Wkly. 2003;133:333–338
14. Klaiman MD, Shrader JA, Danoff JV, et al. Phonophoresis versus ultrasound in the treatment of common musculoskeletal conditions. Med Sci Sports Exerc, 1998; 30:1349–1355
15. Yildiz N, Atalay NS, Gungen GO, et al. Comparison of ultrasound and ketoprofen phonophoresis in the treatment of carpal tunnel syndrome J Back Musculoskelet Rehabil. 2011; 24:39-47
16. Machet L, Boucaud A. Phonophoresis: efficiency, mechanisms and skin tolerance. Int J Pharm. 2002; 243:1–15
17. Windt D, Heijden G, Berg SG, et al. Ultrasound therapy for musculoskeletal disorders: a systematic review. Pain. 1999; 81:257–271
18. García I, Lobo C, López E, et al. Comparative effectiveness of ultrasonophoresis and iontophoresis in impingement syndrome: A double-blind, randomized, placebo controlled trial. Clin Rehabil. Apr 10. pii: 0269215515578293, 2015
19. Boyaci A, Tutoglu A, Boyaci N, et al. Comparison of the efficacy of ketoprofen phonophoresis, ultrasound, and short-wave diathermy in knee osteoarthritis. Rheumatol Int. 2013; 33:2811–2818
20. Luksurapan W, Boonhong J. Effects of phonophoresis of piroxicam and ultrasound on symptomatic knee osteoarthritis. Arch Phys Med Rehabil. 2013; 94:250-5
21. Durmus D, Alayli G, Tufekci T, et al. A randomized placebo-controlled clinical trial of phonophoresis for the treatment of chronic neck pain. Rheumatol Int. 2014; 34:605-11
22. Durmus D, Alayli G, Canturk F. Effects of quadriceps electrical stimulation program on clinical parameters in the patients with knee osteoarthritis. Clin Rheumatol, 2007; 26:674–678
23. Ağargün MY, Tekeoğlu I, Güneş A, et al. Sleep quality and pain threshold in patients with fibromyalgia. Compr Psychiatry. 1999; 40:226-8
24. Beck AT, Ward CH, Mendelson M, et al. An inventory for measuring depression. Arch Gen Psychiatry. 1961; 4:561–571
25. Solomon DH, Bates DW, Panush RS, et al. Costs, outcomes, and patient satisfaction by provider type for patients with rheumatic and musculoskeletal conditions: a critical review of the literature and proposed methodologic standards. Ann Intern Med, 1997; 127:52–60
26. Sarrafzadeh J, Ahmadi A, Yassin M. The effects of pressure release, phonophoresis of hydrocortisone, and ultrasound on upper trapezius latent myofascial trigger point. Arch Phys Med Rehabil. 2012; 93: 72-7
27. Ebadi S, Ansari NN, Henschke N, et al. The effect of continuous ultrasound on chronic low back pain: protocol of a randomized controlled trial. BMC Musculoskeletal Disorders, 2011;12:59
28. Byl NN. The use of ultrasound as an enhancer for transcutaneous drug delivery: phonophoresis. Phys Ther. 1995; 75:539–553

29. Hoppenrath T, Ciccone CD. Is there evidence that phonophoresis is more effective than ultrasound in treating pain associated with lateral epicondylitis. Phys Ther, 2006;86:136–140
30. Sarrafzadeh J, Ahmadi A, Yassin M. The effects of pressure release, phonophoresis of hydrocortisone, and ultrasound on upper trapezius latent myofascial trigger point. Arch Phys Med Rehabil. 2012; 93:72-7
31. Bakhtiary AH, Fatemi E, Emami M, et al. Phonophoresis of Dexamethasone Sodium Phosphate May Manage Pain and Symptoms of Patients with Carpal Tunnel Syndrome. Clin J Pain. 2013;29:348-53
32. Reshetov PP, Tverdokhleb IuP, Bezmenov VA. The use of hydrocortisone combined with ultrasound with gonarthrosis patients. Vopr Kurortol Fizioter Lech Fiz Kult. 2000; Jul-Aug;(4):47-8
33. Mason L, Moore RA, Derry S, et al. Systematic review of topical capsaicin for the treatment of chronic pain. BMJ. 2004; 328(7446):991. Review
34. Laslett L, Jones G. Capsaicin treatment for osteoarthritis pain: A metaanalysis. The Cochrane Central Register of Controlled Trials (CENTRAL) 2015 Issue 12 http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/426/CN 01010426/frame.html accessed 21.03.2016
35. Laslett L, Jones G. Capsaicin for osteoarthritis pain. Prog Drug Res. 2014; 68:277-91,Review
36. Hochberg MC, Altman RD, April KT, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care Res (Hoboken). 2012; 64:465-74
37. Kuptniratsaikul V, Tosayanonda O, Nilganuwong S, Thamalikitkul V. The efficacy of a muscle exercise program to improve functional performance of the knee in patients with osteoarthritis. J Med Assoc Thai. 2012; 85:33–40
38. Pedersen BK, Bruunsgaard H. Possible benefical role of exercise in modulating low-grade inflammation in the elderly, Scand J Med Sci Sports. 2003; 13:56-62
39. Helmark IC, Mikkelsen UR, Borglum J, et al. Exercise increases interleukin- 10 levels both intraarticularly and peri-synovially in patients with knee osteoarthritis: a randomized controlled trial, Arthritis Res Ther. 2010; 12: R126