DICLOFENAC SODIUM PHONOPHORESIS VERSUS CONVENTIONAL THERAPEUTIC ULTRASOUND IN KNEE OSTEOARTHRITIS

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Abstract

Purpose: to compare the effect of diclofenac sodium phonophoresis (DSPH) with conventional therapeutic ultrasound (TUS) on knee OA. Subjects and methods: Fifty patients (two groups) participated in this study. Group (A); consists of 25 patients (5 males, 20 females), with mean age 57 years, treated with TUS plus exercises. Group (B); consists of 25 patients (8 males, 17 females), with mean age 54 years, treated with DSPH plus exercises. Each patient was assessed for knee pain intensity level and physical function using the WOMAC score and knee flexion ROM using the digital inclinometer pretreatment, posttreatment and follow up one month after treatment. Results: There were non-significant differences among group (A) for WOMAC score, and significant only at posttreatment and follow up compared to pretreatment for group (B) (P-value <0.003⁵). Significant differences between posttreatment compared to pretreatment and follow up among group (A) for knee flexion ROM (P-value <0.03⁵), and significant only between post and pretreatment for group (B) (P-value = 0.000⁶). However, there was no significant difference between groups neither at posttreatment nor at follow up. Conclusion: DSPH had improvement but not significant in pain intensity level, physical function, and knee flexion ROM posttreatment but it had no superior effect on TUS. Knee flexion ROM improved significantly posttreatment in both groups, but only in PH the improvement sustained for one month after treatment. PH had long term effect than TUS.

Key words: Knee osteoarthritis, Diclofenac sodium phonophoresis, Therapeutic ultrasound
INTRODUCTION

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 have 50 years and older and may cause physical disability (3). Symptoms of knee OA include stiffness and knee pain limit weight-bearing activities such as walking, going up and down stairs, and standing up from a chair (4). Treatment of knee OA is mainly directed toward reducing joint pain, as well as improving joint mobility (5).

TUS is a deep heating agent that has been widely used to reduce pain in patients with knee OA (6, 7). TUS 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, through thermal mechanism, include elevation of the pain threshold, alteration of neuromuscular activity leading to muscle relaxation, induction of tissue regeneration, and reduction of inflammation (8, 9).

PH is a therapeutic method that uses US to enhance percutaneous transportation of drugs. PH with nonsteroidal anti-inflammatory drugs (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 (10-16). 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 (11).

Diclofenac sodium gel is NSAIDs. It is used for treating pain in certain joints (eg. in the knees or hands) caused by OA (17).

Randomized controlled trial was conducted to compare the effects of DSPH with TUS on pain intensity level, function ability and knee flexion ROM in patients with symptomatic knee pain caused by mild to moderate OA.

SUBJECTS AND METHODS

This study was conducted at the outpatient clinic of orthopedic physiotherapy unit, Cairo University Hospitals, upon approval of Faculty of Physical Therapy, Cairo University, Egypt. The study extended from March 2018 to December 2018.

Each patient was examined by the researcher for the inclusive and exclusive criteria. WOMAC score and ROM of knee flexion were measured pretreatment, posttreatment and, one month after treatment as follow-up. Prior starting of the study each patient signed informed consent. Patients were assigned to two groups randomly.

Subjects

Fifty patients referred by orthopedic surgeons as knee OA participated in this study, with age range from 50 to 65 years (18), from both genders; diagnosed with mild to moderate knee OA according to Kellgren-Lawrence grades (19) and have
body mass index \( \leq 32 \text{ kg/m}^2 \). Patients randomly divided into two groups, 25 patients in each group. **Group (A)** received TUS waves of 1MHz frequency and 1watt/cm\(^2\) was applied to the target knee with Aquasonic gel only. In addition, conventional therapeutic exercises including strengthening exercises for hip abductors and adductors, quadriceps, hamstring muscles, and stretching exercise of hamstring \(^{(20-22)}\). **Group (B)** will receive Ultrasound waves of 1MHz frequency and 1 watt/cm\(^2\) was applied to the target knee with a topical pain relieving gel (1% diclofenac sodium), and the same conventional therapeutic exercises as **Group (A)**.

**Inclusion Criteria**

Patient’s age range from 50 to 65 years old\(^{(18)}\); knee pain off at least 6 months duration; moderate to severe knee pain; self reported restricted range of motion and / or joint deformity of the knee; have grade 2 (minimal) or 3 (moderate) knee OA according to the Kellgren and Lawrence criteria, based on the radiographs\(^{(19)}\); able to walk on their own for 10 minutes.

**Exclusion Criteria**

Concomitant disease affecting the knee, such as rheumatoid arthritis, systemic lupus erythema, psoriatic arthritis; Intra-articular corticosteroid or hyaluronic acid injection into the knee within the last 3 months; arthroscopy of the knee within the past year; significant injury to the knee within the past 6 months; using of assistive device other than a knee support; diseases of spine or other lower extremity joints of sufficient degree to affect assessment and treatment procedures; joint replacement of the involved knee.

**PROCEDURES INSTRUMENTATIONS:**

**Measurements Instrumentations:**

**Digital Inclinometer:** The range of motion (ROM) of the flexion and extension of the target knee measured by digital inclinometer in degrees from prone lying position. Normal knee flexion is 135\(^\circ\) and normal knee extension is 0\(^\circ\).

**Therapeutic Instrumentations:**

Therapeutic ultrasound machine; (Uniphy – phyaction U). Ultrasound unit for all ultrasound therapy applications. Multi-frequency ultrasound head 1 MHz and 3 MHz, 4 cm\(^2\). Acoustic and visual contact control (www.gymna-uniphy.com). 1MHz frequency and 1watt/cm\(^2\) was used in application of continuous US with and without diclofenac sodium.

**MATERIALS**

1. **WOMAC Questionnaire**\(^{(23-25)}\).
2. **Aquasonic gel in Group (A), the skin coated with an Aquasonic gel not containing a pharmacologically active substance. Features:** Acoustically correct for the broad range of frequencies used. Completely aqueous, not stain clothing or damage transducers. Unique "can't be copied" formula is bacteriostatic, non-sensitizing and non-irritating. No formaldehyde. Not a spermicide. It was used and
recommended by leading manufacturers of medical ultrasound equipment worldwide (www.parkerlabs.com/aquasonic-100.asp).

3. (1%) Diclofenac sodium gel preparation In Group (B), 3g of topical gel containing 1% diclofenac sodium applied over the target knee (17). TUS then applied to the superomedial and lateral parts of the knee through the applicator head in circular movements (26).

ASSESSMENT PROCEDURES

All subjects were evaluated for their pain intensity level, stiffness and physical function assessment of the target knee by WOMAC questionnaire (23-25) and knee flexion ROM by a digital inclinometer in degrees from prone lying position. All patients were tested before and after the treatment program with follow-up one month after the treatment.

TREATMENT PROCEDURES

Treatment program: 12 treatment sessions (3 sessions per week for 4 weeks).

1-Therapeutic ultrasound

Group (A) received ultrasound waves of 1MHz frequency and 1watt/cm². Patients were put in a sitting position with the knees 90⁰ flexed. Therapeutic ultrasound was applied to the superomedial and lateral parts of the target knee through the applicator head in circular movements with aquasonic gel only for 5 min (26).

2-Diclofenac Sodium Phonophoresis

Group (B) received ultrasound waves of 1MHz frequency and 1watt/cm². Patients were put in a sitting position with the knees 90⁰ flexed. Therapeutic ultrasound was applied to the superomedial and lateral parts of the target knee through the applicator head in circular movements with a topical pain relieving gel (3g (1%) Diclofenac Sodium) for 5 min (26).

3-Exercises

Active strengthening exercises for quadriceps (sitting knee extension) (27), hamstrings (prone lying), hip abductors (standing & supine lying) and hip adductors muscles (supine lying) 10 repetitions with 3 sets, 6 seconds rest between each repetition, and 1 minute rest between the sets) (20-22).

Stretching exercises for hamstrings and the calf muscles were done (3 repetitions, 30 seconds in position of stretching, 30 seconds in position of relaxation, and 3 repetitions with 3 sets).

DATA ANALYSIS

All statistical analyses were done using SPSS version 18 (IBM Inc., Chicago, IL) with the p-value set at ≤ 0.05. Descriptive statistics are presented as means and SD for all patients. Normality test of data using Shapiro-Wilk test was conducted. Accordingly, repeated measures ANOVA and multiple pairwise comparisons (post hoc test with bonferroni adjustments) were used to compare within groups differences in both dependent variables. Independent t-test was conducted to detect among groups differences in dependent variables and in demographic
data (as assumptions were not all and not very significantly violated). Z test was used to compare proportions of male and female in both groups.

RESULTS

Shapiro-Wilk test reflected that all the data was normally distributed for all data (P<0.05) except age (P=0.04) and BMI. Levene’s test for equality of variances showed non-significance except for posttreatment of WOMAC score, but it did not matter due to equal sample sizes.

General Characteristics of the Subjects:

Group (A): Twenty five (5 males, 20 females) patients were included in this group. Their mean ± SD of age, weight, height, and BMI were 56.8 ± 4.3 years, 73.12 ± 9.85 kg, 1.62 ± 0.013 m, and 28.25 ± 2.8 kg/m² respectively as shown in table (1).

Group (B): Twenty five patients (8 males, 17 females) were included in this group. Their mean ± SD age, weight, height, and BMI were 54.12 ± 5 years, 77.2 ± 8.7 kg, 1.63 ± 0.086 m, and 28.99 ± 3 kg/m² respectively as shown in table (1).

Comparing demographic data between both groups, with independent t-test, revealed non-significant differences.

INFERENTIAL STATISTICS FOR DEPENDENT VARIABLES

A-WOMAC score

1- Among groups differences Group (A) (TUS)

The mean ± SD values of WOMAC score at pretreatment, posttreatment and follow-up were 64.44±19, 54.28 ±23.6, and 53.62 ±15.66 respectively. Repeated measures ANOVA (with Bonferroni adjustment) revealed non-significant differences among pretreatment, posttreatment, and follow up (F=1.9, P-value= 0.2); so no need for multiple pairwise comparisons (post hoc test). See table (2) and figure (1).

Group (B) (PH)

The mean ± SD values of WOMAC score at pretreatment, posttreatment and follow-up were 69.7±14.3, 50.36±13.18, and 52.94±19.87, respectively. Repeated measures ANOVA (with Bonferroni adjustment) revealed significant differences between pretreatment, posttreatment, and follow up (F=23.8, P-value= 0.000*). Multiple pairwise comparisons (post hoc test with bonferroni correction) revealed that there were significant differences of WOMAC score between pre and post treatment (P=0.000*) and between pretreatment and follow up (P-value=0.003*), but not between posttreatment and follow up (P=0.98), see table (1) and figure (1).

<table>
<thead>
<tr>
<th>Table (1)</th>
<th>Comparison of the mean age, weight, height, and BMI of both groups (A, B) and sex distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.8±4.3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73.12±9.85</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>1.62±0.013</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.25±2.839</td>
</tr>
<tr>
<td>Male/female (count)</td>
<td>5/25</td>
</tr>
</tbody>
</table>

Table (2) Multiple pairwise comparison tests (Post hoc tests) for the WOMAC within groups at different measuring periods

<table>
<thead>
<tr>
<th></th>
<th>Prec VS. Post</th>
<th>Prec VS. FU</th>
<th>FU VS. Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (A)</td>
<td>0.26</td>
<td>0.26</td>
<td>1</td>
</tr>
<tr>
<td>Group (B)</td>
<td>0.000*</td>
<td>0.003*</td>
<td>0.98</td>
</tr>
</tbody>
</table>

*Significant at alpha level =0.05
2- Between groups differences
Independent t-test revealed that the mean values of the pretreatment, posttreatment and follow up between groups showed non-significant differences with (P>0.27), see table (2).

<table>
<thead>
<tr>
<th>Group (A) VS. Group (B)</th>
<th>Pre</th>
<th>Post</th>
<th>FU</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-value</td>
<td>0.27</td>
<td>0.48</td>
<td>0.92</td>
</tr>
</tbody>
</table>

B-ROM of knee flexion
1- Among groups differences Group (A) (TUS)
The mean ± SD values of knee flexion ROM at pretreatment, posttreatment and follow up were 106.68±14.07, 117.92±9.46, and 108.23±8.02, respectively. Repeated measures ANOVA (post hoc test with Bonferroni adjustment) revealed significant differences between pre, posttreatment, and follow up (F=10.34, P-value=0.003*).
Multiple pairwise comparisons revealed that there were significant differences in knee flexion ROM between pre and post treatment (P=0.000*), but neither between pretreatment and follow up nor between post treatment and follow up (P>0.66), see table (3) and figure (2).

Group (B) (PH)
The mean ± SD values of knee flexion ROM at pretreatment, post treatment and follow up were 106.08±17.685, 118.44±13.2, and 110.67±24.67, respectively. Repeated measures ANOVA (post hoc test with Bonferroni adjustment) revealed significant differences between pre, post treatment, and follow up (F=15.85, P-value=0.000*).
Multiple pair wise comparisons revealed that there were significant differences in knee flexion ROM between pre and post treatment (P=0.000*), but neither between pretreatment and follow up nor between post treatment and follow up (P>0.66), see table (6) and figure (4).

2- Between groups differences
Independent t-test revealed that the mean values of the pretreatment, posttreatment and follow up between groups showed non-significant differences with (P-value>0.74), see table (4) and figure (2).

DISCUSSION
The main purpose of this study was to compare the effect of DSPH with TUS on knee OA.
The study general hypothesis stated that there would be no significant difference between PH and TUS in treating knee OA patients. The results of this study failed to reject this general hypothesis, as there were non-significant differences between groups at all measuring periods in all dependent variables (WOMAC score and ROM of knee flexion).

WOMAC score (pain intensity level, stiffness, physical function)

It was hypothesized that there would be non-significant difference between PH and TUS in WOMAC score in knee osteoarthritis patients. Findings of the present study revealed that there were non-significant differences among group (A) for WOMAC score, and significant at post treatment and follow up compared to pretreatment for group (B) (P-value < 0.003*), but non-significant between post treatment and follow up.

The current study showed that PH had improvement but not significant effect on pain intensity level and physical function (WOMAC score) of knee osteoarthritis patients. This suggests that PH are important in decreasing pain intensity level and disability in patients with knee OA, fortunately this effect was maintained one month posttreatment (follow up). However, there was non-significant difference between groups, clinical improvements in WOMAC score was found posttreatment in PH group.

The finding of the current study regarding effect of DSPH on WOMAC score agree with Deniz et al. (2009) who found that DSPH had significant effect on pain intensity level and physical function (WOMAC score) in knee OA patients.

The finding of the current study regarding non-significant difference between PH and TUS agree with Kozanoglu, et al. (2003) who found that ibuprofen PH and TUS were effective in reducing pain intensity level and Ibuprofen PH was not superior to conventional TUS in patients with knee OA.

The finding of the current study regarding non-significant difference between PH and TUS agree with Manbark et al (28) (2007) who found non-significant difference between PH and TUS in pain intensity level score and physical function score, but in lateral epicondylitis patients.

Findings of the current study disagree with Akinbo et al. (2011) found a significant improvements in WOMAC score (pain intensity level, stiffness, physical function) and knee flexion ROM using DSPH than TUS. The contrast findings between the present study and that of Akinbo et al. (2011) may be to the sessions in the latter study were daily and used heat and bike without exercises.

The finding of the current study regarding non-significant difference between PH and TUS disagree with Luksurapan and Boonhong (2013) who found that PH was significantly more effective than TUS in reducing pain intensity level and tended to improve knee functioning in knee OA patients. Differences between the present study
and that of Luksurapan and Boonhong (2013) may be due to using longer duration of PH (10 min) without exercises in the latter study.

**Knee flexion range of motion**

It was hypothesized that there would be non-significant difference between PH and TUS in ROM of knee flexion in knee OA patients.

There were significant differences between pre and posttreatment and between post treatment and follow up among group (A) for knee flexion ROM (P-value <0.03), and significant at posttreatment compared to pretreatment for group (B) (P-value = 0.000). However, there was no significant difference between groups neither at posttreatment nor at follow up.

Findings of the present study showed that knee flexion ROM improved but not significant posttreatment, unfortunately this improvement not sustained at one month posttreatment (follow up) for group (A) but in group (B) the improvement sustained for one month posttreatment. This means that PH had long term effect than TUS.

The finding of the current study regarding non-significant difference between PH and TUS in ROM agrees with Moubark et al. (2007) who found that non-significant difference between PH and TUS in ROM, but in lateral epicondylitis patients.

Findings of the current study disagree with Akinbo et al. (2011) found a significant improvements in knee ROM using DSPH than TUS. The contrast findings between the present study and that of Akinbo et al. (2011) may be to the sessions in the latter study were daily and used heat and bike without exercises.

**LIMITATIONS**

This study has a few limitations that should be considered in future research studies:

- Small sample size, due to poor patients' compliance.
- Several patients were illiterate, which might cause difficulties in comprehending the index well.

**CONCLUSION**

DSPH had improvement but not significant in pain intensity level, physical function, and knee flexion ROM posttreatment but it had no superior effect on US. Knee flexion ROM improved significantly posttreatment in both groups, but only in PH the improvement sustained for one month after treatment. PH had long term effect than US.

**RECOMMENDATIONS**

- Further studies are required to investigate.
- How the results of the study might be influenced by using only biophysical modalities without exercises.
- Effect of using objective measures for pain intensity level and physical function.

**REFERENCES**

1990; 65:1214–1221.


27) Kahler A. Top 5 popular knee exercises. Healthy Hippie. 2013 DEC.


Web Resources

- www.gymna-uniphy.com
- www.parkerlabs.com/aquasonic