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The effectiveness of ultrasound treatment for the management of knee osteoarthritis: a randomized, placebo-controlled, double-blind study

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Background/aim: A randomized, placebo-controlled, double-blind study was designed to investigate the effectiveness of ultrasound therapy in primary knee osteoarthritis.

Materials and methods: Ninety patients between 40 and 65 years of age having grade 2 and 3 bilateral knee osteoarthritis enrolled in the study were randomly assigned into 3 groups: continuous ultrasound, pulsed ultrasound, and placebo ultrasound. All patients were given a home exercise program. Patients were evaluated at baseline, at the end of the treatment, and at the second month after the treatment by a range of motion measurement, visual analog scale, Lequesne index for knee osteoarthritis, and Short Form-36 quality of life scale.

Results: The increase in the knee range of motion was similar in both ultrasound groups, while the change in the placebo group was not statistically significant. Visual analog scale scores and Lequesne scores of the placebo group at the second month were significantly greater than both ultrasound groups' scores ($P < 0.01$ and $P < 0.05$, respectively).

Conclusion: Significant improvements in terms of pain, function, and quality of life scales were noted in both ultrasound groups in comparison with the placebo group. No statistically significant difference was found in terms of efficacy between the continuous and pulsed ultrasound.

Key words: Knee osteoarthritis, ultrasound, treatment

1. Introduction

Osteoarthritis (OA) is the most common joint disorder and its incidence increases with age. Although it can affect many joints in body, it mainly affects load-carrying joints (1,2). Treatment of OA aims to reduce joint pain and stiffness, preserve and improve joint mobility, reduce physical limitations, increase the quality of life, prevent further joint damage, and educate patients about the course and results of the disease. Recent guidelines recommend nonpharmacological modalities like training, physical therapy, aerobics, strengthening and aquatic exercises, weight loss, walking aids, thermal modalities, transcutaneous electrical nerve stimulation, and acupuncture. Surgical treatment is applied when conservative methods fail. Ultrasound (US), with its analgesic and antispasmodic effect on muscles, is one of the widely used nonpharmacological treatment methods for OA. US can be applied in 2 different modes, continuous and pulsed. Thermal effects are predominant in continuous mode application, which is advised for the treatment of chronic cases. These thermal effects are augmentation of blood flow, increased capillary permeability, tissue metabolism and fibrous tissue extensibility, muscle relaxation, and elevation of pain threshold. In pulsed mode application, the heat that occurs within the tissue with the first stimuli by US waves disappears until the second stimuli; the mechanical effect and deep penetration in the tissue provide a micromassage effect and the degree of heat in the tissue does not change. Pulsed mode US is preferred for the treatment of acute and subacute cases. The nonthermal effects are chemical activity increase, fluid flow increase, and change in permeability of cell membranes, which all provide analgesic effects (3–5). The literature about comparison of different modes of US therapy in knee OA is lacking and placebo-controlled trials regarding the efficacy of therapeutic US are scarce. The present study aims to examine and compare the effects of continuous and pulsed US treatment on pain, function, and quality of life in patients with knee OA.

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2. Materials and methods

Ninety patients between 40 and 65 years of age consulting the outpatient clinic with the complaint of knee pain, who were diagnosed with bilateral stage 2 and 3 primary knee OA according to Kellgren–Lawrence criteria, were enrolled in the study. Patients with secondary knee OA; active synovitis; symptomatic hip, foot, and ankle disease; neurologic deficits in a lower extremity; recent knee trauma; history of intraarticular steroid and/or hyaluronate injection in the past 6 months; history of knee surgery or arthroscopy to the knee joint in the last year; and application of physical treatment to the knee in the last 3 months were excluded from the study. Written informed consent was obtained from each patient.

Age, sex, body mass index (BMI), duration of disease, profession, and educational levels of the patients were recorded. Patients were evaluated by physical examination and standing anteroposterior and lateral knee roentgenograms. Each knee was staged according to the Kellgren and Lawrence radiological stage (6). Complete blood count, erythrocyte sedimentation rate, urinalysis, C reactive protein, rheumatoid factor, and serum electrolytes were tested.

The study protocol was a randomized, placebo-controlled, double-blind design. Previously prepared and randomly enumerated closed envelopes that contained the treatment methods were used for the randomization. Patients were randomized into 3 groups, each group consisting of 30 patients. In group 1 continuous US (frequency: 1 MHz, intensity: 1.5 W/cm^2, duration: 5 min) and in group 2 pulsed US (frequency: 1 MHz, intensity: 1.5 W/cm^2, mode: 1/5, duration: 5 min) were applied to the anterior, medial, and lateral areas of the knees bilaterally. In the third group placebo US was applied; the patients in this group received exactly the same treatment procedure as the treatment groups, except that the power switch was off. All treatments were applied for 5 days a week for 2 weeks by the same 5-cm^2 head US device (Enraf Nonius Sono plus 492) and physiotherapist. All patients were given a home exercise program at the beginning of the treatment. Patients were instructed to perform the exercise program, including quadriceps isometric exercises and strengthening exercises, for 10 repetitions of the set, 3 times a day for 8 weeks from the beginning of the treatment. To ensure that exercises were learned properly, exercise cards including the exercises were also handed out. The patients were informed that they could take 500 mg of paracetamol up to 3 times a day in case of pain during treatment. The range of motion (ROM) of each knee was recorded; a visual analog scale (VAS) was used to evaluate pain at rest, sleep, and movement; and Lequesne functional index values were recorded at each visit for the evaluation of function. Quality of life evaluation was done using the Short Form-36 (SF-36) and was recorded at baseline and at the second month. The VAS is a scale consisting of 10-cm horizontal lines, with anchor points of 0 (no pain) and 10 (maximum pain). The Lequesne index is a specific evaluation standard developed for patients with knee and hip OA (7) that evaluates maximum walking distance and daily life activities. The SF-36 is one of the most commonly used general health scales, used for a variety of health status requirements, evaluating quality of life.

2.1. Statistics

A statistical package program was used to evaluate the data obtained from the study. Descriptive statistical methods (frequency, proportion, mean, and standard deviation) were used in the evaluation of research data as well as the Kolmogorov–Smirnov distribution test for examining normal distribution. The Pearson chi-square test was used in comparing qualitative data. In comparing quantitative data, the Kruskal–Wallis test was used in intergroup comparison of parameters when there was more than one group and the Mann–Whitney U test was used in determining the group causing a difference. The Wilcoxon test was used for intragroup comparisons. The results were calculated at the 95% confidence interval, $P < 0.05$ significance level, and $P < 0.01$ advanced significance level.

3. Results

No study participant left the research project for any reason. No side effects or complications were observed during the treatment. Baseline characteristics of the patients are shown in Table 1. The continuous US group included 25 female and 5 male patients, the pulsed US group included 24 female and 6 male patients, and the placebo group included 26 female and 4 male patients. The average age was 56.13 ± 6.61 years in the continuous US group, 54.63 ± 6.53 years in the pulsed US group, and 57.76 ± 7.15 years in the placebo group. BMI was found to be 32.31 ± 5.23 in the continuous US group, 31.15 ± 4.68 in the pulsed US group, and 30.91 ± 4.33 in the placebo group. No statistically significant difference was found between the 3 groups in terms of age, BMI, or sex ($P > 0.05$). The number of female patients in all 3 groups was significantly higher than the number of male patients.

No statistically significant difference was found between the knee pain duration of cases in the pulsed US group and the continuous US group ($P > 0.05$). The average duration of pain in the placebo group (5.10 ± 3.62 years) was found to be significantly higher than in the cases in the US groups (2.80 ± 2.31 years) ($P < 0.05$). There was no statistically significant difference between groups in terms of Kellgren and Lawrence radiological stage distribution ($P > 0.05$). For the pulsed US and continuous US groups, the number of patients with stage 3 OA was higher than the ones with stage 2 OA.

Table 1. Baseline characteristics of the patients.

Characteristics	Continuous US (n = 30)	Pulsed US (n = 30)	Placebo (n = 30)	P
Age (years, mean ± SD)	56.13 ± 6.61	54.63 ± 6.53	57.76 ± 7.15	0.264
Duration (years, mean ± SD)	4.10 ± 3.15	2.80 ± 2.31	5.10 ± 3.62	0.028*
BMI (kg/m^2 mean ± SD)	32.31 ± 5.23	31.15 ± 4.68	30.91 ± 4.33	0.632
Sex (female/male)	25/5	24/6	26/4	0.787
Kellgren–Lawrence radiological stage (II/III)	12/18	10/20	16/14	0.279

Data are presented as mean ± SD or number of patients. *P < 0.05.

The increase in active and passive ROM of both knees for the pulsed and continuous US groups at the end of the treatment was statistically significant in comparison to baseline active and passive ROM scores (P < 0.01). Additionally, the increase in active and passive ROM of both knees at the second month after the treatment was statistically significant in comparison to the ROM scores at the end of treatment (P < 0.01). The increase in active and passive ROM at the end of the treatment and at the second month after treatment were similar in the continuous and pulsed US groups (P > 0.05). The active and passive ROM increase in the placebo group at the second month after the treatment was significantly lower than in the continuous and pulsed US groups (P < 0.01). The ROM increase in the placebo group was not statistically significant (P > 0.05).

The decrease in VAS movement scores at the end of the treatment and at the second month after treatment in the US groups was statistically significant (P < 0.01). At the second month after treatment, VAS rest, sleep, and movement scores of the placebo group were significantly greater than both US groups' VAS scores (P < 0.01). No statistically significant difference was found between continuous and pulsed US groups in terms of VAS movement scores in the second month (P > 0.05). In contrast to the US groups, in the placebo group an increase was recorded in VAS movement values at the second month after treatment in comparison to the VAS movement scores at the end of the treatment, and it was statistically significant (P < 0.01) as shown in Table 2.

Continuous and pulsed US groups showed a statistically significant increase in terms of the SF-36 physical component scale at the second month after treatment in comparison to baseline values (P < 0.01). There was no statistically significant difference between US groups. The increase in the second month scores of the placebo group in terms of the SF-36 physical component scale was not statistically significant (P > 0.05).

In terms of the SF-36 mental component scale, there was a statistically significant increase in the continuous and pulsed US groups at the second month after treatment (P < 0.05). In the placebo group, the decrease in mental component scale scores at the second month after treatment in comparison to baseline scores was not statistically significant (P > 0.05).

The decreases in Lequesne pain, walking distance, daily life activity, and index scores in the continuous and pulsed US groups were similar at the second month after treatment. Lequesne pain, walking distance, daily life activity, and index scores for the placebo group were significantly higher than in the continuous and pulsed US groups at the end of the treatment and at the second month after treatment (P < 0.05). The change in the placebo group was not significant, as shown in Table 3.

Table 2. Pain scores.

VAS movement (mm)	Continuous US (n = 30)	Pulsed US (n = 30)	Placebo (n = 30)	P
Baseline	8.97 ± 1.45	8.60 ± 1.61	8.93 ± 1.44	0.598
At the end of the treatment	5.40 ± 1.79	5.17 ± 2.02	6.73 ± 2.89	0.020*
Second month after treatment	3.90 ± 2.54	3.83 ± 2.61	7.20 ± 2.66	0.000**

Data are presented as mean ± SD. *P < 0.05, **P < 0.001.

Table 3. Lequesne index scores during the study.

Lequesne index score	Continuous US (n = 30)	Pulsed US (n = 30)	Placebo (n = 30)	P
Baseline	13.20 ± 3.66	12.90 ± 2.73	12.37 ± 3.68	0.451
At the end of the treatment	8.15 ± 3.35	7.85 ± 2.75	10.50 ± 3.61	0.003**
Second month after treatment	5.45 ± 3.43	6.02 ± 3.14	11.73 ± 4.53	0.000**

Data are presented as mean ± SD. *P < 0.05, **P < 0.001.

4. Discussion

Treatment of OA aims to reduce joint pain and stiffness, preserve and improve joint mobility, reduce physical limitations, increase the quality of life, prevent further joint damage, and educate patients about the course and results of the disease. The use of physical treatment modalities is important due to the considerable gastrointestinal and cardiac side effects of pharmacological agents commonly used in the treatment of OA, which is an important issue especially for the geriatric patients.

US, which is among the most commonly used physical treatment methods, is a deep heating modality with analgesic and antispasmodic effects on muscles. The analgesic efficacy of therapeutic US results from both thermal and nonthermal effects. Thermal effects cause a decrease in pain sensation by affecting tissue metabolism, capillary permeability, pain threshold, and an increase in tissue elasticity. Nonthermal effects decrease pain sensation by stimulating tissue regeneration, changing cell membrane permeability, and increasing the intracellular calcium entrance to the neural system (3). Although US is frequently used in the conservative management of knee osteoarthritis, there is no consensus about mode of application and the few studies in the literature about its therapeutic efficacy report conflicting results.

Commonly observed clinical findings of knee OA are pain, joint stiffness, decrease in ROM, and functional loss (8,9). Knee pain, ROM, and functional indices (SF-36 and Lequesne index) were evaluated in the present study. We detected significant increase in active and passive ROM at the end of the treatment and at the second month in both US groups, whereas no statistical significance was detected between continuous and pulsed US groups in terms of ROM increase. Falconer et al. (10) examined the effectiveness of US on joint stiffness and pain in patients with knee OA and knee contracture. The patients were divided into 2 groups; exercises and US treatment were applied to one group and placebo to the other. A significant recovery was observed in active ROM, pain, and walking speed of both groups, of which the effects lasted for at least 2 months. They found no significant difference between groups in terms of ROM and reported that US treatment had no contribution to exercises in patients with knee OA and chronic knee contracture. The patients in Falconer et al.'s study included patients with chronic knee contractures; 8 of them had total knee arthroplasty, and US was applied for 3 min in duration and the dose was not constant. In contrast to the aforementioned study, our study included no patients with knee contracture and the applied US treatment was at a constant dose for 5 min in duration. We concluded that US treatment is effective in osteoarthritic knees with no contractures in terms of increasing ROM.

Huang et al. examined the effectiveness of US on isokinetic exercises in patients with knee OA. Their study included 120 patients with knee OA who were divided into 4 groups. Isokinetic stretching exercises were applied in the first group, isokinetic stretching exercises and continuous US were applied in the second group, and isokinetic stretching exercises and pulsed US were applied in the third group. The fourth group was a control group. They reported an increase in ROM and walking speed in the second and third groups; the highest recovery rates in terms of walking speed and decrease in disability were achieved in the third group. In conclusion, it was reported that US treatment increased the efficacy of isokinetic exercise and thus the functional improvement in patients with knee OA. In contrast to our study, where we found no difference between continuous and pulsed US groups, Huang et al. reported a superior efficacy of pulsed US (11).

VAS scores at rest, sleep, and movement were evaluated in the current study. Posttreatment VAS scores of the placebo group at all times were significantly higher than in the US groups. Continuous and pulsed US seem to have similar efficacy in terms of pain reduction in knee OA. Özgönelel et al. examined the clinical effects of therapeutic US on patients with knee OA and conducted a randomized, double-blind, placebo-controlled study including 67 patients who were divided into pulsed US treatment and placebo treatment groups. They evaluated the patients at the end of the treatment by the VAS movement scale, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and 50-m walking test. They reported a

statistically significant difference in recovery in the pulsed US group in terms of VAS movement, WOMAC, and 50-m walking test in comparison to the placebo group (12).

The results of the current study are consistent with the results of the aforementioned studies in confirming the superiority of US treatments over placebos in the treatment of knee OA. Our study differs in demonstrating a relatively longer period of efficacy. Most of the investigations regarding the efficacy of therapeutic US on knee OA evaluate the immediate posttreatment results, which gives information about short-term efficacy. Unlike the previous studies we evaluated both posttreatment and relatively long-term (2 months after treatment) results. Clinical findings and symptoms are related to changes occurring in intraarticular and periarticular structures. The deep heating effect of therapeutic US, especially on the periarticular structures, might be responsible for the improvements achieved in patients in the US groups. Obviously, studies with longer follow-ups are needed to evaluate the long-term efficacy of therapeutic US in the management of knee OA.

Kalpakçıoğlu et al. conducted a randomized clinical study, which included 15 patients in 2 groups, and applied isometric quadriceps exercises as well as US treatment for 15 days to one group and short wave diathermy modality to the other. Functional evaluations were made in terms of VAS pain scores and WOMAC index at baseline and at the end of the treatment. Statistically significant improvement was observed in both groups in terms of pain and function, and no significant difference was determined between the 2 groups. US treatment applied together with an isometric quadriceps exercise program resulted in significant recovery in terms of pain and functional state in knee OA, which is consistent with the results of our study (13).

Lequesne pain, walking distance, daily life activity, and index scores for the placebo group were significantly higher than in the continuous and pulsed US groups at the end of the treatment and at the second month after the treatment. The decrease in Lequesne pain, walking distance, daily life activity, and index scores in the continuous and pulsed US groups were similar at the second month after treatment. The change in the placebo group was not significant. The present study demonstrated that both US modalities provided improvement in functional parameters in patients with knee OA, with no superiority between continuous US and pulsed US groups.

In conclusion, application of continuous and pulsed US resulted in significant recovery in terms of pain, functional state, and quality of life in patients with knee OA without obvious superiority between continuous and pulsed US groups. Therapeutic US can be used as a safe and effective physical treatment modality in the management of patients with knee OA. Long-term observation with larger samples is required to investigate the long-term efficacy.

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