

ORIGINAL ARTICLE

Comparison of the Efficacy of Transcutaneous Electrical Nerve Stimulation, Interferential Currents, and Shortwave Diathermy in Knee Osteoarthritis: A Double-Blind, Randomized, Controlled, Multicenter Study

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ABSTRACT. Atamaz FC, Durmaz B, Baydar M, Demircioglu OY, Iyiyapici A, Kuran B, Oncel S, Sendur OF. Comparison of the efficacy of transcutaneous electrical nerve stimulation, interferential currents, and shortwave diathermy in knee osteoarthritis: a double-blind, randomized, controlled, multicenter study. *Arch Phys Med Rehabil* 2012;xx:xxx.

Objective: To compare the effectiveness of transcutaneous electrical nerve stimulation (TENS), interferential currents (IFCs), and shortwave diathermy (SWD) against each other and sham intervention with exercise training and education as a multimodal package.

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

Setting: Departments of physical medicine and rehabilitation in 4 centers.

Participants: Patients (N=203) with knee osteoarthritis (OA).

Interventions: The patients were randomized by the principal center into the following 6 treatment groups: TENS sham, TENS, IFCs sham, IFCs, SWD sham, and SWD. All interventions were applied 5 times a week for 3 weeks. In addition, exercises and an education program were given. The exercises were carried out as part of a home-based training program after 3 weeks' supervised group exercise.

Main Outcome Measures: Primary outcome was a visual analog scale (0–100mm) to assess knee pain. Other outcome measures were time to walk a distance of 15m, range of motion, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Nottingham Health Profile, and paracetamol intake (in grams).

Results: We found a significant decrease in all assessment parameters ($P<.05$), without a significant difference among the groups except WOMAC stiffness score and range of motion. However, the intake of paracetamol was significantly lower in each treatment group when compared with the sham groups at 3 months ($P<.05$). Also, the patients in the IFCs group used a lower amount of paracetamol at 6 months ($P<.05$) in comparison with the IFCs sham group.

Conclusions: Although all groups showed significant improvements, we can suggest that the use of physical therapy agents in knee OA provided additional benefits in improving pain because paracetamol intake was significantly higher in the patients who were treated with 3 sham interventions in addition to exercise and education.

Key Words: Osteoarthritis, knee; Rehabilitation; Transcutaneous electric nerve stimulation.

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OSTEARTHRTIS (OA) has been reported as being a major cause of significant morbidity and an extensive use of health care resources because it is the most common degenerative joint disorder.¹ OA may affect several joints, especially weight-bearing joints, such as the knee, because it is characterized by the deterioration of articular cartilage in the joints.¹⁻³

Although many treatment approaches are widely used in the treatment of knee OA, none of these can completely cure knee OA. According to the guidelines of the American College of Rheumatology⁴ and the Osteoarthritis Research Society International,⁵ current therapies for OA are effective in reduction of pain and secondary functional disability. Physical therapy agents, such as shortwaves and electrotherapeutic approaches, are used for pain relief and reduction of secondary functional disability in treating acute and chronic pain due to knee OA.^{6,7}

Physical therapy agents most widely prescribed by physicians include shortwave diathermy (SWD), transcutaneous electrical nerve stimulation (TENS), and interferential currents (IFCs). These physical therapy agents are claimed to be effective in the management of knee OA. SWD, a form of electromagnetic therapy, produces an oscillating electromagnetic field, which results in movement of ions, distortion of molecules, and creation of eddy currents; subsequently, heat is produced in the deep tissue.⁸ Although SWD can be used to induce an anti-inflammatory response, reduce joint stiffness,

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List of Abbreviations

CI	confidence interval
IFC	interferential current
NHP	Nottingham Health Profile
OA	osteoarthritis
RCT	randomized controlled trial
SWD	shortwave diathermy
TENS	transcutaneous electrical nerve stimulation
VAS	visual analog scale
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

stimulate connective tissue repair, and reduce muscle spasm and pain,⁹⁻¹¹ its efficacy on knee OA is still inconclusive.

On the other hand, as described by Melzack and Wall,¹² TENS and IFCs are forms of electroanalgesia based on the gate control theory of pain perception. According to this theory, stimulation of large diameter (A- β) primary sensory afferent cutaneous fibers activates inhibitory interneurons in the spinal cord dorsal horn and thus may ease the transmission of nociceptive signals from small diameter (A- Δ) and C fibers.¹³ While the active element of TENS is the biphasic pulsed currents,^{14,15} IFCs deliver currents to deep tissues through the use of kilohertz carrier frequency pulses or sinusoidal currents to overcome the impedance offered by the skin. Two currents can be delivered out of phase because very high frequency currents are not uncomfortable for subjects; these currents interfere with each other within tissues at the point where the currents cross.^{16,17} The lack of adequate evidence to support the use of any type of electrotherapy in patients with knee OA can be explained by the inadequacies in the quality and appropriateness of randomized controlled trials (RCTs),¹⁸⁻²¹ although there is some evidence that TENS and IFCs are beneficial for some forms of pain.^{22,23} Therefore, double-blind RCTs with adequate power are necessary to evaluate the effectiveness of these therapy opportunities for the treatment of knee OA. This motivated us to design a double-blind RCT with a multicenter basis in order to investigate the efficacy of SWD, TENS, and IFCs for the management of knee OA.

On the other hand, in order to gain muscle strength, restore injured tissues, and contribute to the ability to sustain everyday life activities, exercise is one of the most frequently used modalities in the rehabilitation of subjects with knee pain. Previous studies have shown that exercise reduces pain and improves function in patients with knee OA.²⁴⁻²⁶ Although there is little evidence to support the use of education in the rehabilitation of knee OA, education together with exercise would help patients adopt an adequate way of coping with symptoms and stimulate functioning, activities, and level of participation, despite pain and stiffness.²⁷ Therefore, the present study set out to investigate the efficacy of TENS, IFCs, and SWD as well as sham intervention with exercise training and education as a multimodal package.

METHODS

Participants and Study Design

This was a double-blind, multicenter, randomized controlled study. Eligible outpatients were aged between 50 and 80 years with knee OA according to American College of Rheumatology criteria, radiologically confirmed with a Kellgren-Lawrence grade of 2 or 3,²⁸ and symptomatic with at least 40mm or 4cm severity of pain on the visual analog scale (VAS) for at least 6 months. Patients were excluded if they had any experience with electrotherapy, had history of any contraindication for electrotherapy, had received corticosteroid therapy or chondroprotective agents during the 30 days prior to the study or viscosupplementation treatment within 6 months prior to the study, or had undergone previous major surgery, such as joint replacement or arthroscopy, within 6 months prior to the study. The other exclusion criteria included a diagnosis of joint infection, a specific condition (neoplasm, diabetes mellitus, paresis, osteonecrosis, recent trauma, etc), ascertained/suspected pregnancy or lactation, and poor general health status that would interfere with the functional assessments during the study. These exclusion criteria were verified by history, physical examination, and radiograph. The study was approved by

the institutional review board at each center, and all participants provided written informed consent.

Randomization was performed by the principal center using adaptive assignment into the following 6 treatment groups, taking into account the subjects' age and sex: TENS sham, TENS, IFC sham, IFC, SWD sham, and SWD. At every patient's first visit to the clinic or hospital, the principal center was contacted and the patient was assigned a unique 2-part number. Patients were screened for eligibility at their second visit, and the principal center was contacted again to allocate a randomization number. All patients, investigators, and analysts were blinded, with the exception of members of the data and safety monitoring board, but these members did not assess patients or participate in the writing of the article.

Treatments

At the beginning of the study, all therapists were instructed to apply the treatments in a standardized way.

Physical therapy agents. Physical therapy agents were applied 5 times a week for 3 weeks by the same physiotherapist at each center. At the end of the study period, each patient was asked to guess the treatment group that he/she was in. This question was to assess the adequacy of our blinding technique.

The TENS (Bio-stim SD-980,^a Endomed CV-405,^b and Sonopuls 492^b) was administered at a frequency of 80Hz with 10- to 30-mA intensity for 20 minutes. Four surface electrodes (5 \times 5cm) were placed over the painful area in the knee region with intensity in the tactile sensation threshold. The patients in the TENS sham group received sham stimulation at the same sites for the same duration and period as the TENS group.

IFCs (Physiomed-IF-Expert,^c Endomed 482,^b and Elektromedizin-ET 3000^d) were applied for 20 minutes with an amplitude-modulated frequency of 100Hz generated by 4-kHz sinusoidal waves. Two electrodes (8 \times 6cm) were placed onto the knee region with intensity in the tactile sensation threshold. The IFC sham treatment consisted of the placement of the same pads for the same time; however, no electrical stimulation was applied to the probes.

In the SWD group, the patients sat on a treatment chair that had an opaque screen between the chair and the SWD machine (Intelect shortwave, Model no. 3812,^e ULTRAMED, 11s601 serial number 3660340,^f and Curapuls 419^b). The screen was used to blind the patient from viewing the procedure being performed on the SWD machine by the physical therapist. Each patient in the treatment group sat on a chair and placed his/her legs on a table during treatment, while receiving continuous SWD with a 10-cm diameter condenser plate operating at a frequency of 27.12MHz, an input of 300W, and a mean output of 3.2W. The SWD sham group received a sham SWD treatment, which had exactly the same treatment procedure as the treatment group, except that the power switch was off.

Exercise program. The exercise program was carried out in groups of 4 or 5 patients under the guidance of a physiotherapist 3 times a week for 3 weeks. After a 5- to 6-minute jogging period, stretching exercises of the lower extremity muscles (~10min) were performed in a standing position. Subsequently, isometric quadriceps exercises (10-15 repetitions) in the seated position, with a towel rolled under the knee, were performed for 10 seconds with 10-second breaks between holds in a progressive manner. Then, chair lift and minisquats exercises (10-15 repetitions) were performed as muscle strength exercises. At the end of the 3-week group exercise period, the physiotherapist prescribed a home-based training program (3 times a week) as well as group exercise. All patients also received a complete set of premade exercise cards showing all exercises, to ensure that the training program

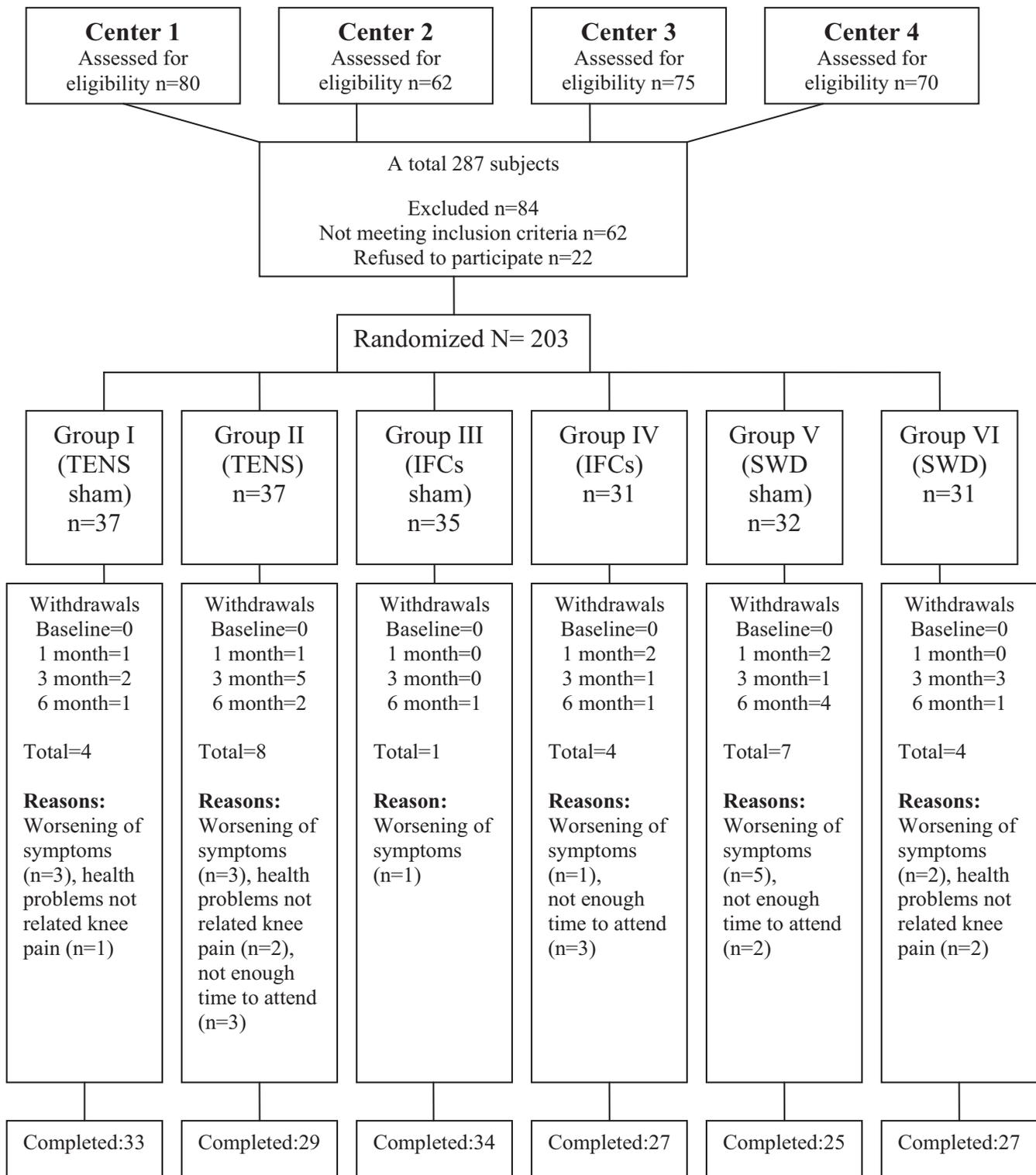


Fig 1. Participant flowchart and assessment.

would be done properly. At each visit during the study, the patients were instructed to perform their exercises regularly.

Education program. Before the treatments, all patients participated in a single education group session (each partici-

pant was given the same computer presentation) of approximately 1-hour duration. This program was given by the physician (1 of the investigators in each center: F.C.A., M.B., O.Y.D., and A.I.). The purpose was to increase patient under-

Table 1: Baseline Demographic Characteristics of Patients

Characteristics	TENS Sham (n=37)	TENS (n=37)	IFCs Sham (n=35)	IFCs (n=31)	SWD Sham (n=32)	SWD (n=31)	P
Age (y)	60.7±6.5	61.9±6.9	61.3±7.8	62.0±7.9	61.4±8.2	61.6±7.4	NS
Sex W/M (%)	27/10 (73.0/27.0)	31/6 (83.8/16.2)	28/7 (80.0/20.0)	27/4 (87.1/12.9)	27/5 (84.4/15.6)	27/4 (87.1/12.9)	NS
BMI (kg/m ²)	29.0±4.1	28.4±3.5	30.4±4.9	29.8±3.4	29.3±3.4	28.5±4.2	NS
Pain duration (mo)	35.4±29.2	44.8±81.7	47.9±46.8	53.2±66.2	39.7±24.5	35.5±28.9	NS

NOTE. Values are mean ± SD or as otherwise indicated.

Abbreviations: BMI, body mass index; M, men; NS, not significant; W, women.

standing of OA, the functional anatomy of the knee, and ergonomic principles, including instructions in daily life activities. Also, treatment approaches and exercises were discussed.

Assessments

Clinical assessments were made at baseline and at months 1, 3, and 6. The physician who assessed the treatment outcomes was unaware of the patient's group of treatment. Primary outcome was a 100-mm VAS to assess knee pain. The patients were asked to make an assessment of their pain between 0 (no pain) and 100 (severe pain). The VAS also measured the patients' satisfaction with their treatment experience, with 0 reflecting extremely dissatisfied and 100 reflecting extremely satisfied.

The active, pain-free range of motion of both knees was measured by a goniometer (only flexion was measured because none of the patients had restriction of extension); time to walk a distance of 15m (s) was measured with a stopwatch.

The patients were asked to discontinue any pretreatment with nonsteroidal anti-inflammatory drugs 7 days before the start of the study. If the patient required additional analgesic medication due to knee pain, paracetamol use was permitted with a condition that they noted paracetamol intake on the study form. At each clinic visit, the study report form was evaluated, and paracetamol intake was recorded in grams.

In addition to clinical assessments, patients were evaluated using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)²⁹ and the Nottingham Health Profile (NHP)³⁰ at baseline and months 1, 3, and 6.

Sample Size

According to the Cochrane review in TENS of knee OA, treatment response was defined as a 50% improvement in VAS pain scores, which corresponds to an average decrease of 1.2 SD units.²³ The sample size was calculated at 28 per group with 80% power to detect a difference of 50% improvement in VAS pain scores with a 2-sided significance level ($P < .05$), and allows for a 30% dropout rate.

Statistical Analysis

Statistical analysis was based on the intention-to-treat approach. Comparison analysis was performed between treatment groups by a one-way analysis of variance. Each treatment group was compared with its sham group by using a paired *t* test. The repeated-measures analysis of variance was used to evaluate the time of observation for the clinical assessment parameters. The Bonferroni test as a post hoc test was used to determine the change between groups. Statistical analyses were performed with the 13.0 Statistical Package for the Social Sciences (SPSS).⁹ All the results were expressed as mean ± SD. A *P* value of $< .05$ was considered statistically significant. In addition, standardized effect sizes (Cohen *d*) with 95%

confidence intervals (CIs) were calculated as a difference between mean scores divided by the pooled SD.³¹

RESULTS

Figure 1 summarizes the patient recruitment, participation, and attrition during the study. No complications occurred as a result of the treatments given. None of the patients who completed the study reported any complaints leading to noncompliance for the home-based exercise program at each visit. None of the patients received other therapy, except the intake of paracetamol, during follow-up. There were no significant differences among the groups at baseline (table 1).

Comparison of Treatment Groups

Table 2 shows the patients' clinical characteristics related to pain. Compared with baseline, during the study, a significant decrease was found in these pain assessment parameters in all treatment groups ($P < .05$, $d > -1.0$), without a significant difference among the groups. As shown in table 3, significant improvement in functions, assessed by the WOMAC function scale (*d* values -0.5 , -0.6 , and -0.7 in the TENS group; -0.5 , -0.6 , and -0.6 in the IFCs group; and -0.7 , -0.7 , and -0.9 in the SWD group), 15-m walking time (*d* values -0.3 , -0.2 , and -0.2 in the TENS group; -0.3 , -0.4 , and -0.5 in the IFCs group; and -0.7 , -0.9 , and -0.9 in the SWD group), and NHP physical mobility scale (*d* values -0.4 , -0.3 , and -0.3 in the TENS group; -0.4 , -0.6 , and -0.5 in the IFCs group; and -0.4 , -0.6 , and -0.6 in the SWD group), was seen in all groups during follow-up ($P < .05$), again with no significant differences among the groups. A similar trend was found for other domains of the NHP. All the treatment groups showed a significant improvement ($P < .05$).

There was also no difference concerning the patients' satisfaction with treatment.

The results of paracetamol intake are reported in figure 2. At 1-month follow-up, paracetamol intake was significantly lower in the IFCs group when compared with the TENS group ($P = .03$; 95% CI, 0.6–14.1), while no further difference was found.

Paired Comparisons (Treatment vs Sham)

When comparing each treatment group with its sham group, no significant difference was found in the clinical assessment parameters (see tables 2 and 3). All sham groups showed significant improvement in pain and function assessments ($P < .05$). However, the intake of paracetamol was significantly lower in each treatment group when compared with its sham group during the first 3 months, as shown in figure 2 ($P < .05$). The patients treated with IFCs also used a significantly lower amount of paracetamol at 6 months ($P = .003$, 95% CI, 7.3–32.7).

Table 2: Patients' Clinical Characteristics Related With Pain During the Study

Characteristics	TENS Sham (n=37)	TENS (n=37)	<i>P</i> [*]	IFCs Sham (n=35)	IFCs (n=31)	<i>P</i> [†]	SWD Sham (n=32)	SWD (n=31)	<i>P</i> [‡]	<i>P</i> [§]
VAS pain										
At baseline	74.4±16.4	76.1±16.2		80.0±18.6	74.4±16.7		80.0±18.5	78.5±15.6		
1mo	50.4±20.3	54.7±24.1	1.00	60.2±27.2	50.4±20.6	1.00	54.0±25.6	49.8±23.7	1.00	0.28
Mean difference	24	21.3		19.8	24		26	28.7		
95% CI	18.1–29.9	15.5–27.1		13.0–26.6	17.6–30.4		18.4–33.6	20.7–36.7		
Effect size (<i>d</i>)	-1.7	-1.0		-0.8	-1.3		-1.2	-1.4		
3mo	47.3±22.6	51.5±24.8	0.56	57.0±23.8	46.2±22.6	1.00	50.2±25.0	48.4±20.4	1.00	0.56
Mean difference	27.1	24.6		23	28.2		29.8	30		
95% CI	20.4–33.7	17.2–32.0		17.0–29.0	20.7–35.6		22.0–37.7	22.3–37.8		
Effect size (<i>d</i>)	-1.4	-1.2		-1.1	-1.4		-1.4	-1.6		
6mo	48.4±22.7	48.6±23.1	1.00	60.3±27.0	46.7±25.2	1.00	50.8±23.2	52.8±23.4	1.00	0.92
Mean difference	25.9	27.4		19.6	29.2		29.2	25.7		
95% CI	18.5–33.4	20.2–34.6		13.8–25.5	21.5–36.9		21.5–36.9	17.8–33.6		
Effect size (<i>d</i>)	-1.3	-1.4		-1.0	-1.4		-1.4	-1.4		
WOMAC pain										
At baseline	14.5±4.0	14.0±4.3		14.8±3.3	13.6±4.3		13.7±3.8	14.0±4.5		
1mo	12.3±5.0	10.9±4.9	1.00	12.0±4.1	10.9±4.5	1.00	10.7±4.6	10.0±5.3	1.00	0.20
Mean difference	2.2	3		2.7	2.7		3.1	4.1		
95% CI	1.3–3.1	2.1–3.9		1.8–3.7	1.8–3.6		1.9–4.2	3.6–5.5		
Effect size (<i>d</i>)	0.0	-0.7		-0.7	-0.6		-0.7	-0.8		
3mo	11.7±5.6	10.4±4.9	1.00	11.1±4.1	10.3±4.5	1.00	10.1±4.9	9.1±4.7	1.00	0.11
Mean difference	2.8	3.6		3.6	3.3		3.6	4.9		
95% CI	1.7–3.9	2.6–4.5		2.6–4.6	2.2–4.4		2.4–4.8	3.5–6.3		
Effect size (<i>d</i>)	-0.6	-0.8		-0.9	-0.8		-0.8	-1.1		
6mo	11.5±5.4	10.2±5.0	1.00	11.5±4.2	10.2±4.3	1.00	10.2±4.8	9.5±5.1	1.00	0.41
Mean difference	3	3.7		3.2	3.4		3.5	4.5		
95% CI	1.8–4.2	2.7–4.7		2.2–4.3	2.2–4.6		2.2–4.8	3.1–5.9		
Effect size (<i>d</i>)	-0.6	-0.8		-0.8	-0.8		-0.8	-0.9		
NHP pain										
At baseline	61.5±24.4	65.1±22.6		75.9±20.0	67.8±25.6		74.3±24.3	71.9±24.9		
1mo	48.4±25.6	45.1±22.2	1.00	54.6±24.6	46.9±24.3	1.00	49.5±22.4	41.1±29.0	1.00	0.16
Mean difference	13.1	20		21.3	20.9		24.9	30.7		
95% CI	5.2–21.1	12.5–27.4		13.5–29.1	12.4–29.4		17.1–32.6	20.3–40.8		
Effect size (<i>d</i>)	-0.5	-0.9		-1.0	-0.8		-1.1	-1.1		
3mo	41.4±25.7	41.8±25.4	1.00	49.8±27.1	44.4±24.3	1.00	43.8±23.7	37.7±25.5	1.00	0.19
Mean difference	20.1	23.3		26.1	23.3		30.5	34.1		
95% CI	10.7–29.5	15.1–31.5		17.4–34.8	13.3–33.4		21.6–39.5	23.0–45.2		
Effect size (<i>d</i>)	-0.8	-1.0		-1.1	-1.0		-1.3	-1.4		
6mo	40.1±25.4	40.8±25.8	1.00	49.6±26.6	42.1±24.8	1.00	43.0±24.4	34.2±24.9	1.00	0.11
Mean difference	21.4	24.3		26.3	25.6		31.3	37.6		
95% CI	11.9–30.9	16.3–32.3		18.0–34.5	15.1–36.2		31.8–40.8	26.4–48.8		
Effect size (<i>d</i>)	-0.9	-0.9		-1.1	-1.0		-1.3	-1.5		

NOTE. The repeated-measures analysis of variance. Values are mean ± SD or as otherwise indicated.

*Comparison of groups of TENS sham and TENS.

†Comparison of groups of IFCs sham and IFCs.

‡Comparison of groups of SWD sham and SWD.

§Comparison of groups of treatment groups.

Stiffness, as assessed by the WOMAC, did not change in either group during the study. Similarly, we did not find a change in the range of motion measurements.

DISCUSSION

This randomized, controlled, multicenter study comparing the effectiveness of TENS, IFCs, and SWD against each other and the sham groups in addition to exercise training and education in knee OA showed that all assessment parameters significantly improved in all groups without a significant difference. However, because paracetamol intake was significantly higher in patients treated with the 3 sham interventions in addition to exercise and education, it can be suggested that

the use of physical therapy agents in knee OA provided additional benefit in improving pain.

Different physical therapy approaches have been suggested to improve the clinical course of knee OA, but the evidence for effectiveness has not been sufficient based on randomized controlled studies. TENS is a frequently used modality in clinical practice and scientific investigations; however, even the results of trials comparing any type of transcutaneous electrostimulation with a placebo or nonintervention control indicate a lack of adequately sized, methodologically sound, and appropriately reported trials. For example, a few studies performed intention-to-treat analysis even though the rates of withdrawals or dropouts were

Table 3: Patients' Clinical Characteristics Related With Function During the Study

Characteristics	TENS Sham (n=37)	TENS (n=37)	<i>P</i> [*]	IFCs Sham (n=35)	IFCs (n=31)	<i>P</i> [†]	SWD Sham (n=32)	SWD (n=31)	<i>P</i> [‡]	<i>P</i> [§]
WOMAC function										
At baseline	43.4±11.7	41.3±13.1		45.3±11.8	42.7±12.9		41.2±10.7	41.1±10.7		
1mo	36.4±12.4	33.9±14.2	1.00	37.0±14.1	36.3±14.2	1.00	33.9±13.2	32.5±12.9	1.00	0.6
Mean difference	7	7.5		8.3	6.4		7.3	8.7		
95% CI	4.8 to 9.1	3.9 to 11.0		4.9 to 11.7	3.8 to 9.2		4.5 to 14.0	5.7 to 11.6		
Effect size (<i>d</i>)	-0.6	-0.5		-0.6	-0.5		-0.6	-0.7		
3mo	34.0±13.8	32.6±13.8	1.00	34.3±11.8	34.6±14.6	1.00	30.9±14.1	29.7±13.5	1.00	0.47
Mean difference	9.4	8.7		11	8.1		10.3	11.4		
95% CI	5.9 to 12.8	5.0 to 12.5		8.0 to 13.9	4.2 to 12.0		6.6 to 14.0	7.1 to 15.8		
Effect size (<i>d</i>)	-0.7	-0.6		-0.9	-0.6		-0.8	-0.9		
6mo	34.3±14.0	31.8±14.9	1.00	33.8±10.5	34.2±13.8	1.00	31.2±13.9	31.2±12.1	1.00	0.88
Mean difference	9.1	9.5		11.5	8.5		9.9	9.9		
95% CI	5.6 to 12.5	5.8 to 13.2		8.5 to 14.5	4.6 to 12.4		6.4 to 13.4	5.3 to -14.6		
Effect size (<i>d</i>)	-0.7	-0.7		-1.0	-0.6		-0.8	-0.9		
Time to 15m (s)										
At baseline	15.3±3.0	15.3±3.8		17.8±7.1	17.4±3.7		16.6±5.2	16.7±5.4		
1mo	14.9±4.4	14.3±3.3	1.00	17.1±7.9	16.2±3.4	1.00	15.5±4.9	15.3±3.2	1.00	0.83
Mean difference	0.5	0.9		0.7	1.2		1.00	1.4		
95% CI	-0.5 to 1.4	0.1 to 1.8		-0.3 to 1.8	0.3 to 2.1		0.6 to 1.7	-0.2 to 3.0		
Effect size (<i>d</i>)	-0.1	-0.3		-0.1	-0.3		-0.2	-0.3		
3mo	14.8±4.4	14.7±3.6	1.00	15.8±5.3	16.1±3.7	1.00	15.5±4.6	14.8±3.3	1.00	0.24
Mean difference	0.6	0.6		2	1.3		1.2	2		
95% CI	-0.5 to 1.7	-0.4 to 1.5		0.2 to 3.8	0.1 to 2.5		0.5 to 1.9	0.3 to 3.8		
Effect size (<i>d</i>)	-0.2	-0.2		-0.3	-0.4		-0.2	-0.4		
6mo	14.8±3.0	14.4±3.5	1.00	16.3±6.3	15.5±4.5	1.00	15.5±5.2	14.1±3.5	1.00	0.15
Mean difference	0.5	0.8		1.5	1.9		1.1	2.6		
95% CI	-0.2 to 1.3	-0.1 to 1.7		-0.2 to 3.3	0.4 to 3.4		0.5 to 1.8	0.9 to 4.4		
Effect size (<i>d</i>)	-0.2	-0.2		-0.2	-0.5		-0.2	-0.6		
NHP physical mobility										
At baseline	48.3±20.8	42.3±18.5		47.9±23.6	44.4±24.8		47.5±20.4	42.9±20.0		
1mo	36.7±23.2	34.9±17.7	1.00	39.3±25.5	34.9±18.7	1.00	36.3±14.4	33.0±22.6	1.00	0.86
Mean difference	11.6	7.4		8.6	9.5		11.2	9.9		
95% CI	6.5 to 16.6	0.8 to 14.1		4.4 to 12.8	0.8 to 18.1		5.5 to 16.9	4.9 to 14.9		
Effect size (<i>d</i>)	-0.5	-0.4		-0.3	-0.4		-0.6	-0.4		
3mo	36.3±23.2	36.6±16.8	1.00	34.9±26.2	30.8±17.7	1.00	31.3±16.1	32.1±19.5	1.00	0.33
Mean difference	12	5.8		13	13 13.6		16.2	10.9		
95% CI	6.6 to 17.4	-1.1 to 12.7		7.3 to 18.7	3.5 to 23.7		8.9 to 23.5	4.7 to 17.0		
Effect size (<i>d</i>)	-0.5	-0.3		-0.5	-0.6		-0.9	-0.6		
6mo	37.1±20.6	36.1±18.1	1.00	34.1±25.8	33.0±19.1	1.00	30.2±15.7	31.1±16.4	1.00	0.55
Mean difference	11.3	6.3		13.8	13 11.4		17.9	11.8		
95% CI	5.8 to 16.7	-1.3 to 13.8		6.0 to 21.7	1.2 to 21.5		10.3 to 25.4	4.8 to 18.9		
Effect size (<i>d</i>)	-0.5	-0.3		-0.6	-0.5		-1.0	-0.6		

NOTE. The repeated-measures analysis of variance. Values are mean ± SD or as otherwise indicated.

*Comparison of groups of TENS sham and TENS.

†Comparison of groups of IFCs sham and IFCs.

‡Comparison of groups of SWD sham and SWD.

§Comparison of groups of treatment groups.

relatively high.²³ In most of the studies, it is not clear whether the patients were adequately blinded. Although blinding is difficult to achieve due to the sensory differences between treatment and sham in such studies, as well as unintended communication between patient and evaluator,³² we believe that the inclusion of patients who had no experience with electrotherapy can allow blinding of the patients. Moreover, Rutjes et al²¹ reported that blinding of patients was adequate if a sham intervention was used that was identical in appearance to the control intervention. To our knowledge, we have found only 1 multicenter study that compares the efficacy of TENS with placebo in knee OA.

However, this study comprised a total of 39 patients in 2 centers with a follow-up of 10 days.³³

Regarding the efficacy of IFCs in knee OA, there are 3 studies that compare the efficacy of IFCs with sham intervention in knee OA,³⁴⁻³⁶ although these studies failed to include controls to adjust for sham effects. First, for the study of Itoh et al,³⁶ it is not clear whether IFCs or TENS was applied to patients, raising some doubts about the conclusions of the study.²³ Second, blinding is arguable in these studies because the investigators did not express whether their patients had prior experience with electrotherapy.^{37,38} Moreover, all 3 studies only include evaluation of

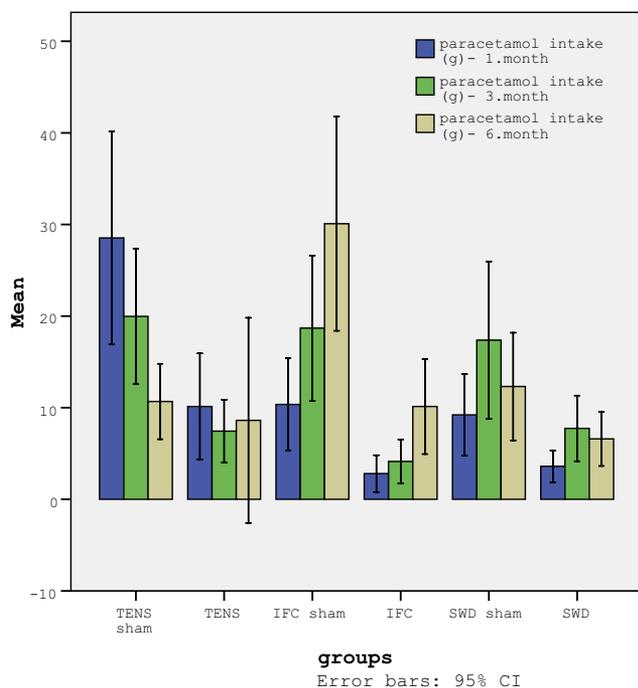


Fig 2. The paracetamol intake in grams [g] during the study.

global pain by using a VAS, without any functional outcome measure.³⁴⁻³⁶

On the other hand, the studies including SWD are limited in evaluating its benefit in addition to exercise in knee OA. Although RCTs are available concerning its effectiveness, their follow-ups are limited because clinical assessments were carried out only at baseline and at the end of the treatment.³⁹⁻⁴¹ Actually, in the literature, the follow-up period was usually short in the studies of all physical therapy agents in knee OA. Another conclusion is that the number of patients studied was relatively small. Against this background, our study is, to our knowledge, the first randomized, controlled, multicenter, well-planned study with a long follow-up period comparing the effectiveness of SWD, TENS, and IFCs in knee OA.

Results showed that both knee pain and function assessment parameters were improved in all groups. Considering the design of the study, these results were not a surprise because exercise training and an education program were given to all patients. An important finding revealed in our study was the issue of pain relief and improved disability by use of the education and exercise program, supporting previous data.^{5,24-27} However, we found that supplementation of physical therapy agents did not reveal an additional benefit during follow-up. Even the patients who were given sham treatments were as satisfied as the patients in groups with physical therapy agents.

Regarding the clinical importance of the differences between the treatment groups, 1 measure used in the literature is Cohen *d* for effect size (difference between mean scores divided by the pooled SD³¹). For the primary outcome measure, Cohen *d* was higher than -1.0 for all treatment groups during follow-up. Sham groups also showed similar *d* values. Cohen defined a small effect size as 0.2, a medium effect size 0.5, and a large effect size as 0.8. Thus, the VAS scores showed a large effect size at months 1, 3, and 6.

In previous data, many studies found that the patients in the sham group showed significant improvement when compared with baseline values.³⁹⁻⁴³ Although it was suggested that the sham effect could be attributable to various factors such as age, diagnosis, study design, therapist and patient relationship, or cultural differences, as reported in the study of Johnson and Din,⁴⁴ we cannot conclude the effect of sham intervention on pain relief because all the patients, even in sham groups, were given exercise training and an education program.

Despite a significant improvement in all groups, the intake of paracetamol was significantly higher in the sham groups for the first 3 months, suggesting that a combination treatment of physical therapy agents, exercise, and education is a more effective intervention for the management of knee OA, with some advantages in pain relief over exercise and education alone. Considering that the difference in the intake of paracetamol between the treatment and sham groups was maintained throughout follow-up in the patients treated with IFCs, it can be interpreted that analgesic effects of IFCs were not only in the short-term.

Another conclusion can be addressed that no difference was found among the treatment groups regarding pain relief, except a significant difference between TENS and IFC effects at month 1. Although the analgesic effects produced by IFCs were similar in magnitude to those observed for TENS in previous data,^{17,45} we found only 1 study comparing the effects of SWD with electrotherapy agents.⁴¹ Cetin et al⁴¹ reported that using physical agents before isokinetic exercises in women with knee OA leads to augmented exercise performance, reduced pain, and improved function without the effects of TENS and SWD. Although the different effect mechanisms of these agents are widely known, the main objective is to use them for reducing pain. Our results supported their benefits in decreasing patients' pain.

Study Limitations

Our study has several limitations. First, we cannot conclude whether physical therapy agents without education and exercise have similar effects on improvement for knee pain, because there was no group consisting of use of physical therapy agents alone. This result suggests that further trials may be needed to elucidate the effect of physical therapy agents. Second, our follow-up period was relatively short. However, when compared with the follow-up periods of the studies of physical therapy agents on knee OA, it seems that our follow-up period was sufficient. However, we believe that the follow-up period of a study on knee OA should be as long as possible in order to assess the efficacy of an intervention.

CONCLUSIONS

Although all groups showed significant improvements, paracetamol intake was significantly lower in the patients who were treated with physical therapy agents. This result supports the hypothesis that a combination treatment of a physical therapy agent, exercise, and an education program as a multidisciplinary intervention has the best outcome in patients with knee OA. On the other hand, we could not find that different physical therapy agents, including TENS, IFCs, and SWD, influenced the results, supporting that various physical therapy agents can be used for pain relief. Nevertheless, our results need to be confirmed by further controlled studies on a wider population in order to establish their definitive effectiveness.

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