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Original Article

Effects of pulsed therapeutic ultrasound on the treatment of people with knee osteoarthritis

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Abstract. [Purpose] The aim was to evaluate the effect of therapeutic ultrasound on the pain, joint mobility, muscle strength, physical function, and quality of life of people with knee OA. [Subjects and Methods] One-site, one-arm, before-after study that included people with Grade II or III tibiofemoral osteoarthritis. Ten therapeutic ultrasound sessions (duty cycle=20%, ERA=10 cm^2, BNR=6:1, SATP=2.2 W/cm^2, SATA=0.44 W/cm^2, frequency=1 MHz, time=4 minutes) were applied. Assessments of primary outcome variables: pain intensity and function, and secondary variables: joint mobility, muscle strength and quality of life, were performed at onset and end of therapy; an additional intermediate evaluation was included for the primary variables. [Results] Means of repeated measurements of pain intensity (pain at rest, pain on palpation and pain after functional activities) and function showed significant differences. There was a significant reduction in pain intensity at the end of functional activities as well as a significant increase in function and in quadriceps muscle strength. [Conclusion] Therapeutic ultrasound applied in accordance with the parameters used, could be recommended during the treatment of individuals with knee osteoarthritis, because it significantly decreased the intensity of pain after the 5th session, and this reduction was maintained until the end of the intervention.

Key words: Pain, Ultrasound therapy, Muscle strength

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INTRODUCTION

Osteoarthritis (OA) is a chronic and degenerative disorder, characterized by joint cartilage wear. Its main symptoms include pain and reduction of joint mobility and muscle strength. It is one of the conditions with the greatest impact on function and quality of life of the elderly in developed countries[1)].

In the United States of America (USA), OA affects 12.1% of the adult population, particularly females (RR=1.79)[2)]. In Colombia, the Ministry of Social Protection reported that healthy life-years (HLY, an epidemiological indicator) lost prematurely due to disability and death were similar to HLY lost due to prostate and cervix cancer and leukemia[3)]. The support joint with the highest incidence of OA is the knee with an incidence of 240 new cases per 100,000 person-years compared to hip OA with an incidence of 88 new cases per 100,000 person-years[4)].

Pain, the main symptom, is present in 38–68% of people with OA and it is associated with insomnia, depression and impairment of participation in social activities[3)]. Moreover, pain has a negative impact on muscle strength and joint Range of

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Motion (ROM), favoring the progressive decline of function and therefore of the quality of life of these people[3].

Therapeutic ultrasound (TUS) is one of the most-used physical modalities of physiotherapy for treatment of knee and hip OA[5]; however, its application has not shown conclusive effects due to methodological limitations such as small sample size, confounding biases and the lack of clarity about the application parameters, the way ultrasound is generated and the recommended dose for this pathology[6].

Few studies[7, 8] have been applied the TUS as the only modality of intervention and evaluated its short-term effects of TUS. These authors did not report significant differences in the variables evaluated possibly due to the application of continuous TUS and by methodological limitations such as selection bias, mainly. Regarding the use of pulsed TUS, only a controlled clinical trial included this form of generation in patients with knee OA. Huang et al.[9] Reported a significant increase in the ROM of the knee, and decreased pain intensity, however, these authors did not evaluate the short-term effect of TUS.

Therefore, considering the high prevalence of OA in the elderly population and the daily use of TUS in clinical practice, the aim of the present study was to evaluate the effect of TUS applied to the medial and lateral compartments of the knee on pain intensity, joint ROM, muscle strength, function and quality of life of the participants. This study was proposed with the hypothesis that relief of pain might increase knee ROM and the strength of the quadriceps and ischiotibial muscles, and hence give rise to a positive change in the function and quality of life of the participants.

SUBJECTS AND METHODS

This A quasi-experimental study with pre and post-intervention analysis included a population of individuals (40–75 years old) with a diagnosis of grade II or III knee (tibiofemoral joint) OA, in accordance with the Kellgren-Lawrence radiographic grading scale, taking into account that in these degrees of severity the ultrasound could be effective[9]. The severity of disease was radiologically evaluated by an orthopedic knee specialist with 23 years of clinical experience.

Individuals were excluded from the study in accordance with the following criteria: if they had received an intra-articular injection of hyaluronic acid or corticoids during the six months prior to the study, or if they had a clinical history of orthopedic knee surgery, a skin disorder, acute-phase respiratory conditions, cardiovascular diseases, such as acute myocardial infarction, during the previous month, or uncontrolled arterial hypertension, or if they had been receiving another kind of physiotherapeutic treatment.

Sample size was calculated considering a power of 80%, a 20% adjustment for follow-up losses, and assuming a significance level of 5%. It was determined that a final sample size of 17 participants would be appropriate for establishing the proposed differences.

The project was approved by the Scientific Research Ethics Committee of the School of Health of Universidad Industrial de Santander with code 7083, and it was carried out in accordance with Good Clinical Practice rules and the Ethics Principles for Medical Research Involving Human Beings that are defined in the latest revision of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to the study.

The number of therapeutic ultrasound sessions (0, 5 or 10) was the explanatory variable of this study. Accordingly, the phases of the evaluation process were defined as initial: at the onset (baseline) of trial (T0); intermediate: at the end of the fifth session (T1); and final: a day after the tenth session of therapeutic ultrasound (T2).

The primary outcome variables were function, intensity of pain at rest (PAR), intensity of pain on palpation (POP), and intensity of pain at the end of a functional activity, specifically the Six-Minute Walk Test (6MWT). This variables were assessed in the T0, T1 and T2 phases. The secondary outcome variables were joint mobility, muscle strength and quality of life of the participants, which were evaluated in the T0 and T2 phases.

Anthropometric and socio-demographic variables, analgesic ingestion, type of analgesic used, level of physical activity, unilateral or bilateral OA, and disease severity score were considered as covariates in the present study.

Before the first session, participants were involved in a process to familiarize them with the instruments and the evaluation tests. During the first session, the initial baseline (T0) assessment was made in the following sequence: First, completion of self-reporting instruments for measuring quality of life (Outcome Osteoathritis Knee Hip Quality of Life/OOAKHQOL[10], PAR, and POP). Then, evaluation of knee flexion and extension ROM, quadriceps and ischiotibial muscles strengths, and performance of the 6MWT were measured. Immediately after the initial evaluation, the first TUS session was applied.

With the aim of ensuring the precision of the measurements, all the instruments and tests used for evaluation were subjected to intra-evaluator and test-retest reproducibility analyses during a previous pilot trial. The intraclass correlation coefficients (ICC) were between 0.93 and 0.97 for intra-evaluator reproducibility of goniometry and hand-held dynamometry, and between 0.82 and 0.97 for a good test-retest reproducibility of the Visual Analogue Scale (VAS), the 6MWT, and the OOAKHQOL instrument.

PAR, POP and intensity of pain after the 6MWT were evaluated using a VAS. This instrument consists of a continuous horizontal line with endpoints labeled with verbal descriptors for defining the limits of the painfulness experience, from “no pain” to “the worst pain experienced,” respectively[11]. Participants were asked to mark with an X the point that represented the intensity of the pain they had on the day of the test.

POP was evaluated after palpation in the medial region (insertion of the *pes anserinus*/goose’s foot tendon), lateral region (femoral condyle, over the insertion of the *fascia lata*), antero-inferior region (tibial tuberosity, over the insertion of the

quadriceps tendon), and posterior region (popliteal fossa) of the knee. Intensity of pain after the 6MWT was assessed immediately after the 6MWT had been performed.

Knee flexion-extension ROM was evaluated with a universal plastic 0–180° goniometer with two 30-cm long arms (Int Standar Goniometer. SEC, Company Orthopaedic Ltd.), in accordance with the recommendations of Norkin and White[12]. This measurement was made twice and the greater value was recorded as the joint ROM and was measured at intervals of 1 or 5 degrees.

Quadricep and ischiotibial muscle strength was measured in pounds (lb) using a manual dynamometer (Microfet 2 model, Hoggan Health Industries Inc.), following the manufacturer's instructions and the recommendations of Kendall and Kendall[13]. Three measurements were taken at 1-minute intervals, and their average was recorded as the muscle strength.

Function was assessed using the 6MWT following the protocol proposed by the American Thoracic Society[14] This test has been used to measure functional state in the elderly[15]. The test was conducted in a 30-meter-long flat and straight indoor hallway which was marked with tape at the start and finish lines and every three meters to facilitate the measure of the distance covered by the individual. The time was controlled using a digital chronometer, and at the end of the test the number of meters walked was recorded.

The information was recorded by a physical therapist with six years of clinical experience who is a candidate for a Master's degree in Physiotherapy.

Quality of life was evaluated by applying the OOAKHQOL, an instrument specifically used for hip and knee OA. This is comprised of 43 items, 40 of which evaluate five attributes: physical activity, mental health, pain, social support, and social activities −and three of which evaluate independent attributes. The scoring of the instrument gives five results, one for each attribute on a scale from 0 (the worst quality of life) to 100 (the best quality of life)[10].

The intermediate (T1) evaluation was performed on the sixth day of treatment, before application of TUS, and included PAR, POP, intensity of pain after the 6MWT, and function. The final evaluation (T2) was performed on the day after the 10th session of treatment and included all variables of the study, as previously described.

The procedures for evaluation of the variables in every participant were carried out at the same time of day, to avoid variations due to circadian rhythm. All of the measurements were made by a physical therapist with 10 years of experience in the musculoskeletal area who is a candidate for a Master's degree in Physiotherapy

The body region to be treated was marked out with a 4-cm wide × 8-cm long template, twice as large as the head of the TUS equipment. The center of the template was placed over the inter-articular line, between the distal end of the femur and the proximal end of the tibia. This template was used during the intervention sessions for all participants.

The therapeutic ultrasound equipment (Sonicator® 730 model, Mettler Electronics,) was calibrated in accordance with IEC (International Electrotechnical Commission) Standard 6116, before using it in the study. The following were the parameters used for treatment: pulsed ultrasound with a duty cycle=20%, ERA=10 cm^2, BNR=6:1, SATP intensity=2.2 W/cm^2, frequency=1 MHz, time=4 minutes and SATA=0.44 W/cm^2. The target body area was twice the ERA of the ultrasound equipment head, and was marked out on the medial and lateral compartments of the knee. In accordance with those parameters, energy of 1,056 J was applied to the medial and lateral compartments of the knee, in each session.

The treatment consisted of 10 sessions—one session a day, five days a week, for two weeks. During the application of therapeutic ultrasound, participants were in a supine position. A 10 cm^3 topical gel without any active pharmacological component was used as a coupling medium. Therapeutic ultrasound was applied with longitudinal movements at the speed set by a metronome operating at 40 bits per minute.

The distributions of outcome variables were evaluated in rating scales using the Shapiro-Wilk test. TUS induced changes in intensity of pain and function were compared between the baseline and the 5th and 10th sessions (T0, T1 and T2) by repeated measures ANOVA. Outcome variables between the starting and the finishing phases were compared using the Student's paired t test, except for intensity of pain after the 6MWT, joint mobility at extension and function, which were evaluated with the Wilcoxon rank test because of their non-parametric distribution.

Bland-Altman agreement limits and their respective confidence intervals (CI) were calculated for every variable of interest to establish the cut-off points for significance of changes attributable to the intervention and not to variance of measurements. The higher value of the upper CI for the Bland-Altman agreement limit was chosen as cut-off point for those variables expected to decrease after treatment, such as PAR, POP and intensity of pain after the 6MWT. The lower value of the lower CI for the Bland-Altman agreement limit was chosen as cut-off point for those variables expected to increase after treatment, such as joint mobility, muscle strength, function and quality of life (Table 1).

The database was prepared in duplicate using Microsoft Excel (2013). The validation of the database and analysis of information were carried out with Stata 12 software (StataCorp. 2011. Stata: Release 12. Statistical Software. The College Station, TX: StataCorp LP) at a significance level of α=0.05.

The present study included 17 participants, (Fig. 1), 70.5% females; mean age: 61.4 ± 6 years. Four individuals had unilateral knee OA, and thirteen had bilateral knee OA. Only the most compromised knee was included in the analysis of individuals with bilateral knee OA

Table 1. Cut-off points of outcome variables of the study

	Variable	Cut-off point
VAS (mm)	Rest	26.7
	Palpation	38.4
	End of functional activities	17.0
ROM (°)	Flexion	30.5
	Extension	7.6
Muscle strength (lb)	Quadriceps	5.2
	Ischiotibials	6.2
6WMT (m)		16.1
OOAKHQOL (0–100)	Physical activity	21.7
	Pain	27.2
	Mental health status	28.4
	Social support	44.7
	Social activities	73.5

VAS: Visual Analogue Scale; ROM: Range of Motion; 6WMT: Six-Minute Walk Test; OOAKHQOL: Osteoathritis Knee Hip Quality of Life; mm: millimeter; ° degrees Celsius; lb: pound; m: meter

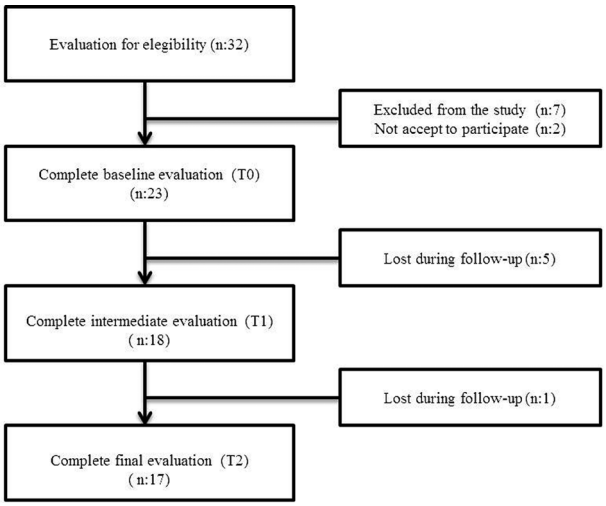

Fig. 1. Flow chart of participants through the phases of the study

Table 2. Features of participants at baseline

	Feature	Total (%) n=17(100)
Sociodemographic	Gender	
	Male	5 (29.4)
	Female	12 (70.5)
	Average age	61.4 ± 6*
Socioeconomic status	Low 2–3	9 (47)
	Medium/High 4–5	8 (52.9)
Schooling	Primary	6 (35.2)
	Secondary	4 (23.5)
	Technical/ University	7 (41.1)
Anthropometric	BMI	
	Not overweight (BMI 25)	2 (11.7)
	Overweight (BM >25 and <30)	6 (35.2)
	Obesity (BM >30)	9 (52.9)
Dominant extremity	Right	14 (82.3)
	Left	3 (17.6)
Involvement	Unilateral	4 (23.5)
	Bilateral	13 (76.4)
Ingestion of analgesics	Yes	11 (64.8)
	No	6 (35.2)
Type of analgesics	NSAIDs	5 (29.4)
	Non-NSAIDs	2 (11.7)
	Opioids	0
	Other	4 (23.5)
	None	6 (35.2)
Level of physical activity (%)	Low	6 (35.2)
	Moderate	6 (35.2)
	Vigorous	5 (29.4)
Severity of OA	Grade ll	11 (64.7)
	Grade lll	6 (35.3)
Patellofemoral OA	Present	16 (94.1)
	Absent	1 (5.8)

*Median ± standard deviation (SD), BMI: body mass index; n: sample size

Table 3. Intensity of pain and function at three moments of evaluation (n=17)

Variable		T0	T1	T2	p**
Intensity (mm)	Rest	35.2 ± 25.5	16.8 ± 15.8	11.8 ± 9.7	0.03
	Palpation	42.1 ± 28.7	18.5 ± 14.1	15.5 ± 12.3	0.004
	End of functional activities	43.6 ± 24.8	25.1 ± 15.9	22.5 ± 22.8	0.07
Function (m)		436 ± 111.2	451 ± 77	490 ± 72.3	0.0001

Median ± SD, mm: millimeters, ** Greinhouse

Table 4. Differences between outcome variables at baseline (T0) and the end (T2) of treatment (n=17)

Variable		T0	T2	p
Intensity of pain (mm)	Rest	35.2 ± 25.5	11.8 ± 9.7	0.0006‡
	Palpation	42.1 ± 28.7	15.5 ± 12.3	0.0005‡
	After the 6MWT	45 (25–67)*	12 (10–34)	0.006‡
Function (m)		449.3 (422.5–465.3)*	484.6 (473.1–512.3)	0.008‡
Joint mobility (°)	Flexion	132 ± 5.0	132 ± 6.1	0.6
	Extension	130 (120–135)	130 (125–135)	0.1
Muscle strength (lb)	Quadriceps	33 ± 10.2	38.3 ± 7.5	0.04‡
	Ischiotibials	24 ± 5.3	25.5 ± 4.1	0.1
Quality of life	Physical activity	47.4 ± 17.2	67.4 ± 19.0	0.0001
	Pain	40.7 ± 24.4	67.4 ± 23.8	0.0001
	Mental health status	52.6 ± 21.3	71.3 ± 17.1	0.0001
	Social support	67.3 ± 19.7	67.3 ± 24.2	0.9

Median ± SD; * Median (ranges 25–75%), mm: millimeters: m: meters, (°): grades, ‡Significant differences in accordance with cut-off points

RESULTS

The main characteristics of participants at the onset of the study are shown in Table 2.

A significant decrease in PAR and POP, as well as improvement in function, were found at the three moments evaluated ($p<0.03$) (Table 3). Moreover, there was a significant decrease in intensity of pain after the 6MWT ($p<0.01$) and a notable increase in function when baseline and final evaluations were compared ($p<0.01$) (Table 4).

No changes in joint mobility or quality of life of the participants were observed ($p>0.05$). Quadriceps muscle strength increased significantly based on the established cut-off points (Table 4).

DISCUSSION

This study was proposed with the hypothesis that relief of pain might increase knee ROM and the strength of the quadriceps and ischiotibial muscles, and hence give rise to a positive change in the function and quality of life of the participants. For this reason, the aim of the research was to evaluate the effect of therapeutic pulsed ultrasound on PAR, POP and intensity of pain after the 6MWT.

Five sessions of TUS, applied in accordance with the parameters described above, significantly decreased the intensity of pain, although there was no change in function. These results suggest that function may be influenced by other variables, such as muscle strength and joint mobility[16], which were not evaluated at T1. Moreover, age-related comorbidities could bias the observed results.

The findings related to relief of pain were higher than those reported by Cakir et al.[17] and Tascioglu et al[18]. They applied ten sessions of therapeutic pulsed ultrasound and found a clinical and statistically significant decrease in PAR and at movements of 28.8 mm and 24.3 mm, respectively. However, these authors evaluated the intensity of pain in accordance with a self-reporting form based on symptoms during the week previous to the evaluation. This might have biased the classification because previous experiences of pain may be associated with their emotional and cognitive aspects, thereby influencing the results[19].

In contrast to the studies mentioned above, the present study evaluated pain immediately after finishing a functional activity, specifically the 6MWT. This is an appropriate evaluation taking into account that pain in people with knee OA could be exacerbated during weight-bearing activities such as walking[20]. This is a variable that should be considered when assessing the post-treatment outcomes in this population.

The post-treatment reduction of intensity of pain after the 6MWT, observed in this study, is likely related to a therapeutic effect of ultrasound on patellofemoral OA, given that the joint is quite near the lateral and medial sides of knee where ultrasound was applied[20]. Additional support for this hypothesis arises from the observation that patellofemoral OA was

present in 94.1% of participants, and it is well known that it is a main source of pain in these persons[20].

The decrease in POP could be influenced by the effect of TUS on soft tissues in the treated region. The knee zone targeted for treatment was comprised of the interarticular line, the tibiofemoral joint, and tissues such as the goose's foot tendon, the iliotibial band and the collateral ligaments, all of which are tissues that tend to be inflamed and painful in people with knee OA. Because of their high collagen content, those tissues have a high ultrasound energy absorption coefficient[21, 22].

The mechanisms by which TUS could be effective for decreasing pain in patients with knee OA are not well defined, but could be related to a decrease in function of the sodium/potassium pump in the pain conduction fibers[23], an increase in membrane permeability which favors a higher vascularization of tissues that are being repaired[24], and a decrease in nitric oxide synthase, which promotes inflammation and chronicity of pain[25]. However, these mechanisms were not evaluated in the present study. The assessment of these physiological mechanisms *in vitro,* and *in vivo* in animal models, is necessary.

With respect to joint mobility, flexion-extension of knee was in the range of 0–135° in the baseline of the study. This range is considered normal for the study population[26], and was unlikely to improve.

Assessment of muscle strength showed significant differences in quadriceps strength at the end of the intervention. This result could be attributable to a reverse effect of TUS over the inhibited muscle. Published studies show that during chronic pathological joint processes, such as OA, the excitability of spinal and supraspinal reflex pathways is impaired, causing limitation in the activation of alpha motoneurons (α-MN) of the joint-related muscles; this, in turn, produces a continuous reflex inhibition of the muscle, known as arthrogenic muscle inhibition (AMI)[27].

Hence, the application of TUS and the associated tissue micro-massage it produces[28] potentially adjust the afferents of Pacinian mechanoreceptors and of free nervous terminations, reversing the inhibition of pathway *Ib*, facilitating the activation of α-MN and the recruitment of muscle fibers, thereby increasing muscle strength[27]. However, the reviewed literature does not contain any studies about the effects of TUS on AMI, and the variables assessed in the present study do not corroborate that hypothesis. Future studies could verify the effect of ultrasound on the activation of the quadriceps muscle through analysis of the H-Reflex and the central activation ratio.

Additionally, the firm contact between the skin and the device head, and its movement over the therapy-targeted zone might activate length-change-sensitive receptors located in the muscle. This in turn would increase the afferents of the *Ia* pathway, favoring the gamma-alpha stimulation which improves complete muscle activation[27]. Future random clinical trials could include a placebo group to verify the proposed mechanism.

The effect of TUS on quadriceps muscle strength has only been studied by Huang et al[9]. They analyzed this effect after application of a pulsed ultrasound protocol and found a significant increase in muscle strength. However, in that study, participants were subjected to a quadriceps muscle strengthening program together with the ultrasound intervention, so those results are not comparable to the ones observed in the present work.

The increased muscle strength after treatment, observed in this work, has clinical relevance, taking into account that a decrease in quadriceps muscle strength is considered to be a predictive factor of the progression of OA[29], a risk factor for knee arthroplasty and a predictive factor of function after knee arthroplasty. The present results showed that participants had an average 0.25 kgf/kg gain in their quadriceps muscle strength at the end of the ultrasound intervention. This might denote a functional improvement and a lower risk of the need for a walking orthosis[30]. In the present study, the results of quadriceps muscle strength correspond to the functional improvement of the participants (Table 3).

No change was recorded in the quality of life at the end of therapeutic ultrasound intervention. This might be explained by the multidimensional nature of this variable and the difficulty of assessing the perception a person has of how each one of those dimensions impacts his/her life. For this reason, it is difficult to track the changes of those dimensions in response to ultrasound treatment, especially when only 10 sessions were applied to treat a disease that is chronic. It is likely that studies with a greater number of treatment sessions will produce significant changes in the quality of life of people with knee OA.

The results of this study indicate that therapeutic ultrasound applied in accordance with the parameters used, could be recommended during the treatment of individuals with knee OA, because it significantly decreased the PAR, POP and intensity of pain after the 6MWT, after the 5th session, and this reduction was maintained until the end of the intervention. Moreover, ten sessions of treatment notably increased quadriceps muscle strength, what could contribute to an increase in the function of the participants.

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