Intrasound Therapy is an Effective Adjunct in the Management of Osteoarthritis of the Knee: A Randomized Control Trial

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ABSTRACT: Intrasound therapy (IST) has been found to improve healing in acute injuries in animal models but no clinical study has been conducted on chronic degenerative conditions in human subjects. The purpose of this study was to investigate and compare the effects of IST and transcutaneous electrical nerve stimulation (TENS) in the management of knee osteoarthritis. Twenty-four patients were randomly assigned into three groups: IST, TENS, and the control group. Subjects in Group 1 had low-intensity IST for 10 minutes and closed-chain exercises, Group 2 subjects had TENS at a frequency of 100 Hz, a pulse width of 150 μs, continuous mode for 15 minutes and closed-chain exercises, while the control group patients had only closed-chain exercises. Treatment was given for eight weeks, twice weekly. Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores, the distance covered in the 6-minute walk test, and knee range of motion were evaluated before and after the treatment. Data were analyzed using paired *t*-test and analysis of variance. Level of significance was set at $P < 0.05$. The clinical outcome measures improved significantly in the posttreatment of the three groups. Subjects in the three groups had significant differences in the mean change in the outcome variables for the WOMAC score (TENS = 29.13 ± 3.83; IST = 28.0 ± 1.72; and control = 13.71 ± 2.52). The post hoc analysis between IST and TENS showed no significant differences but IST had better clinical outcome than TENS.The results of this study suggest that IST may be an alternative to TENS as an adjunct therapy in the management of osteoarthritis of the knee.

KEYWORDS: knee osteoarthritis, WOMAC index, 6-MWT, intrasound therapy, TENS, closed-chain exercises

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Introduction

Osteoarthritis (OA) is a chronic localized joint disease and a leading cause of musculoskeletal pain and disability. The knees, followed by the hips, are the most commonly affected weight-bearing joints in the body.[1] Diracoglu et al.[2] described OA as the most commonly encountered musculoskeletal anomaly, and it has been documented that those suffering from it use healthcare services at a higher rate than individuals with other chronic conditions.[3]

The main clinical symptoms associated with knee OA include pain, articular stiffness, crepitation, articular edema, joint deformities and decrease in range of motion (ROM), physical activity limitations, and muscle weakness.[4,5]

There is currently no cure for OA, and treatment options may be nonpharmacological, pharmacological, or surgical. Currently, there are no drugs that have addressed the degenerative problem but only to treat the pain caused by the disease.[6,7] Clinical guidelines advocate conservative nonpharmacological strategies such as exercises which is a popular treatment option given the ease of application, limited potential adverse effects, and relatively low costs.[8,9] This may be accompanied by other electrophysical modalities that have been proven to be beneficial in the management of individuals with OA.

Physiotherapy is one of the professions that provide effective nonpharmacological interventions for people with knee OA[10] through several means, which include kinesiotherapy, a modality that comprises different types of therapeutic exercises, such as stretching, strengthening, and aerobic exercises.[11] Additionally, electrotherapeutic modalities such as therapeutic ultrasound (TUS) and transcutaneous electrical nerve stimulation (TENS) are included.[12,13]

On the other hand, intrasound therapy (IST) is a relatively novel treatment modality in physiotherapy, and there is a dearth of clinical trials on its efficacy in the management of knee OA. The intrasound vibrator massager produces mixed frequency acoustic waves in the intrasonic range (16,000–20,000 Hz), and there are claims of its efficacy in the management of a wide range of ailments, including improved healing in acute inflammatory injuries.[14] Prior studies also found it to be effective and superior to low-intensity pulsed ultrasound in

tendon healing when used in animal models.[15,16] The intrasound machine has simplicity of operation as it does not have complicated choices of treatment parameters when compared with other electrophysical gadgets such as TENS. The intensity is increased by turning the radial knob anti-clockwise and can be given at any comfortable intensity for the patient.[16,17] There have been subjective reports of the IST as being beneficial in ameliorating the symptoms associated with knee OA, but there is a dearth of clinical trials to ascertain this. This work was therefore a preliminary study to investigate the therapeutic effects of intrasound in OA knee.

The purpose of this study was to determine the effects of IST on Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores, 6-minute walk test (6-MWT), and knee ROM in individuals with OA of the knee, comparing it with other physical modalities such as TENS, which has been found to be effective in ameliorating the symptoms accompanying knee OA.[18] The results of this study will serve as primary investigations into the effects of IST on the symptoms associated with OA and offer the possibility of IST being used as an adjunct therapy in the management of OA knee.

Materials and Methods

Subject selection. A total of 32 subjects (eight males and 24 females; mean age of 62.3 years; range 52–76) were recruited for the study. They were all referred to the Physiotherapy Outpatient Clinic of the Lagos University Teaching Hospital, Idi-Araba, Lagos.

The subjects were assessed by obtaining a detailed history and by carrying out physical examinations and radiographic assessment. Information relating to age, sex, weight, height, duration of knee pain, and past and present medications were collected from the patients.

Of the 32 patients, two were found ineligible for the study and were excluded. The eligible subjects were randomly assigned into three groups through a consecutive sampling technique. Each group consisted of 10 patients (a total of 30 patients); however, 24 subjects completed the study (eight males and 16 females). Reasons for withdrawal by the six subjects who did not complete the study are given in Figure 1.

All the patients included in this study were diagnosed of unilateral OA of the knee and continued with their medications. Excluded were patients with underlying systemic diseases, other rheumatic conditions of the knee and patients with severe OA using the Kellgren and Lawrence[19] system of classification. Approval was sought and obtained from the Research and Ethics Committee of the Lagos University Teaching Hospital (LUTH) prior to the commencement of the study with the assigned approval number of ADM/DCST/HREC/1806. The research was conducted in accordance with the principles of the Declaration of Helsinki.

After satisfying the inclusion criteria, the subjects were fully incorporated into the study following given written informed consent duly signed by the subjects.

A nonprobability consecutive sampling technique was employed. The subjects who met the inclusion criteria were recruited as they became available.

Intervention protocol. The subjects were randomly assigned into three groups by an independent assessor using a computer-generated randomization. Group 1 (the control group) comprised subjects who were treated using closed-chain exercises only. Group 2 comprised subjects who were treated using IST and closed-chain exercises, while Group 3 received both TENS and closed-chain exercises.

A basal medical examination was performed before the commencement of the treatment, and OA diagnostic evaluation based on symptoms and conventional anteroposterior knee radiographs was done. Prior to the commencement of the intervention, all the participants underwent assessment and evaluations for perceived health and physical function with the WOMAC Questionnaire, ROM with a universal goniometer, and functional exercise capacity using the 6-MWT. After this, all the patients were subjected to an eight-week treatment intervention, twice per week, on nonconsecutive days.

The participants were instructed to arrive at the clinic in a rested and fully hydrated state, having not consumed caffeine in the previous four hours and to avoid strenuous exercises in the 48 hours preceding a session. To minimize the effects of diurnal biological variation, all the treatments were performed at the same time of the day.

Treatment protocol. *Group 1 (control).* The subjects in the control group were engaged in the following kinematic exercises (which the subjects in other groups also participated in):

Bicycle ergometry. The bicycle ergometer was ridden by each of the subjects for 20 minutes at their own speed.

Cybex machine. This was used purposely for strengthening the quadriceps and the flexor compartment (hamstrings) of the thigh, the patient lifts the attached arm of the machine with the ankle with the resistance adjusted by the knobs. After 10 repetitions, the legs were changed and the whole procedure was repeated.

Wobble board standing. This was to improve the balance and proprioception of the patients. The wobble board was placed inside the parallel bar with a mirror in front (for biofeedback). The patients held on to the parallel bar to achieve stability and gradually let go of the bars and stood unsupported. This was done for 10 minutes.

Squatting exercise. The patients were instructed to place their backs against the wall, with the head, buttocks, and the heels of their feet touching the wall, and then, the patients bent the knees to ~45°. They were in that position for 10 seconds after which they relaxed and took deep breaths intermittently. This was repeated five times.

Range of motion exercises. This was done to increase the ROM of the knee joint. The patient were asked to lie supine, and patella mobilization and soft tissue massage were performed with the use of topical analgesic cream, and the knee was slowly moved through the available ROM.

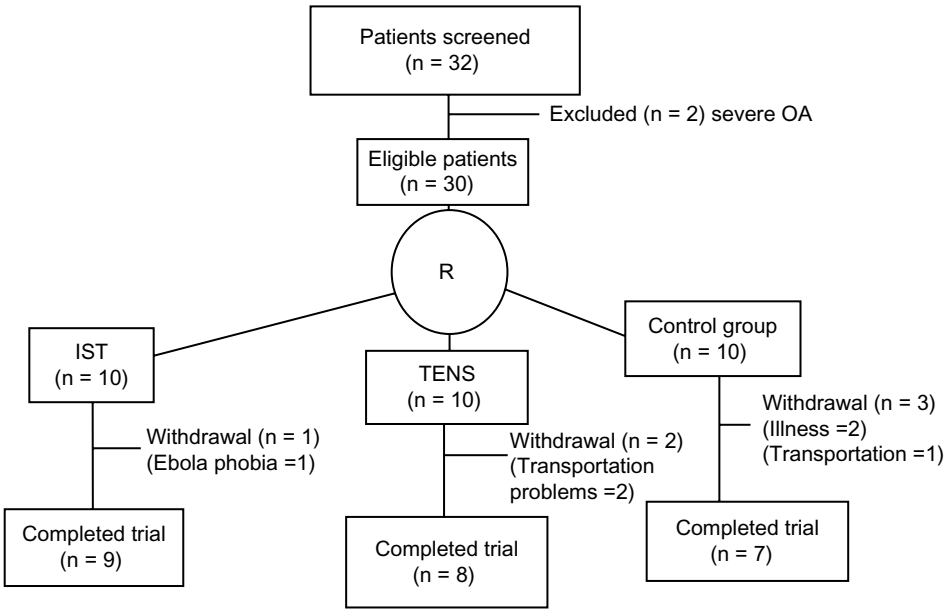


Figure 1. Flow chart of patients through the study.
Abbreviation: R, randomization; TENS, transcutaneous electrical nerve stimulation; IST, intrasound therapy; OA, osteoarthritis.

Group 2. Subjects were positioned supine on a plinth with the knee supported by a pillow at ~15° from full knee extension, which is a relaxed position for the knee joint.

The skin of the subjects was cleaned with methylated spirit prior to commencement of the stimulation. The procedure was explained to the subjects and the expected sensation at the first treatment session.

The intrasound massager was plugged in, set at the most comfortable intensity for the subject[16] and moved over the affected part of the knee joint in circular motion for 10 minutes with KY-Jelly as a coupling medium. The subjects reported a fine feeling of micromassage and vibrations during the procedure. The patients were monitored for any adverse reaction to the IST treatment, but none was reported. Afterward, the subjects were given the same closed-chain exercises that were given to the subjects in the control group.

Group 3. The subjects were asked to lie in supine position on a plinth with the knee supported by a pillow at ~15° from full knee extension. Four rubber electrodes (4 cm × 4 cm) from a dual channel TENS unit were used. The skin of the subjects' was cleaned with methylated spirit to prepare the knees for stimulation; the skin was moistened with a damp cloth prior to application of electrodes in order to improve the electrode adhesion.

The subjects were educated about the procedure at the first treatment session.

The TENS device was set up, and the self-adhesive electrodes plugged to the terminals of the TENS device and attached to the patients' knee in coplanar.

The parameters were set at a frequency of 100 Hz, a pulse width of 150 µs, continuous mode, and time duration of 15 minutes. The intensity was adjusted to the level that was comfortable for the patients (subjects reported a mild-to-moderate feeling of sensation, which was not unbearable during the course of the procedure). The subjects were thereafter given the same closed-chain exercises that were given to the subjects in the control group.

Outcome measures. Baseline assessment was carried out prior to the commencement of the intervention.

Pain intensity assessment. This was assessed using the pain scale of the WOMAC Osteoarthritis index LK3.1 (IK).[20] The scale has five questions or items, each graded from 0 (none) to 4 (extreme). Each subject was instructed to pick within the range that best described their perception of pain for each of the activities as directed by the questionnaire.

Assessment of stiffness level. This was assessed using the stiffness scale of the WOMAC Osteoarthritis index.[20] The scale has two questions or items, each graded from 0 (none) to 4 (extreme). Each subject was instructed to pick within the range that best described the level of stiffness for each of the activities as directed by the questionnaire.

Functional level assessment. This was done using the difficulty in performing daily activities scale of the WOMAC Osteoarthritis index LK3.1 (IK).[20] This subscale has 17 questions or items relating to the level of physical function, each graded from 0 (none) to 4 (extreme). Each subject was instructed to pick within the range that best answered the question. The total scores were used to determine the level of physical function of the participants. The same was done for pain and stiffness level.

Body mass index. The weight was measured in kilograms and recorded to the nearest 0.1 kg and the height in meters. The BMI was obtained by dividing the weight in kilograms by the square of the patient's height in meters; it was documented as kg/m^2.

Range of motion. The patient was in supine position (half lying) with hip flexed ~45°, knee fully extended, fulcrum of the goniometer centered over the lateral epicondyle of the femur, stationary arm aligned with the lateral femur in line with the greater trochanter, and moving arm aligned with the lateral fibula in line with the lateral malleolus. The subject was then told to move the knee actively to his/her limit with the moving arm being moved with the leg. Measurement was then read to the nearest degree.

6-Minute walk test. The participants were asked to walk at their usual pace or at a comfortable pace as far as possible using the 19 m taped floor of the gymnasium at the Physiotherapy Department, LUTH. Subjects were instructed prior to the test to wear comfortable clothing and shoes and to use their typical walking aid during the test. The subject went through the 19 m distance, with the Assistant researcher timing for six minutes, after which the subject was stopped and the total distance covered was recorded in meters.

Data analysis. Statistical Package for Social Science (SPSS Inc.) 21.0 version for Windows package program was used to analyze the data. Demographic and quantitative data were expressed as mean ± standard deviation (SD) and confidence interval to describe the differences in related treatments; the effect sizes were calculated between the means divided by the pooled SD.

The pretreatment values of the outcome measures analyzed were limited only to the patients who completed the study.

Paired sample *t*-test was used to compare the baseline/pretreatment and posttreatment variations in outcome variables in each group. One-way analysis of variance (ANOVA) was used to detect any statistically significant differences in the (improvement) changes between the three groups (exercise vs IRT vs TENS). A post hoc evaluation of ANOVA using the least significant difference was carried out to compare the mean changes between the three groups in order to detect where statistical differences existed and which treatment was statistically more effective.

Required information was extracted from the WOMAC Questionnaire; the information was computed in tables and figures showing the frequencies and percentages.

All the data were presented as mean ± SD. The *P*-value was set at a value of <0.05.

Results

A total of 24 patients participated in the study; nine patients were recruited in the IST group, eight patients in the TENS, and seven patients in the control group. The mean age was 62.3 ± 7.7 years with more than half of the sample size over 60 years of age.

A total of eight males and 16 females (16) participated in this study. Of the 24 participants, five participants were within the normal BMI range (<25 kg/m^2), seven participants were overweight (25–29 kg/m^2), while 12 participants were obese (≥ 30 kg/m^2).

The baseline characteristics are given in Table 1. Comparison of baseline mean values using ANOVA revealed that there were no significant differences in baseline characteristics in the groups except with respect to age ($P = 0.04$).

According to Table 2, analysis of clinical outcome measures of patients in the three groups pre- and postintervention shows significant differences regarding improvement in changes in primary (WOMAC scores) and secondary outcome measures (ROM, 6-MWT) in TENS, IST, and the control group ($P < 0.05$).

Figure 2 shows appreciable improvements in the mean changes pre- and posttreatment in all the outcome measure parameters in the IST and TENS groups when compared with the control group except for the 6-MWT. Table 3, however, shows no significant differences when the changes in the parameters are compared between the IST and TENS groups.

Discussion

This study presents the first clinical trial on the efficacy of IST and comparing it with other proven therapeutic modalities. The

Table 1. Baseline characteristics of the patients.

	IST MEAN ± SD	TENS MEAN ± SD	CONTROL GROUP MEAN ± SD	F-VALUES	*P*-VALUE
Age	66.22 ± 8.00	57.13 ± 5.50	63.00 ± 6.88	3.715	0.042*
BMI (kg/m^2)	30.75 ± 4.12	29.10 ± 5.67	26.45 ± 6.67	1.221	0.315
6-MWT	297.50 ± 67.04	302.50 ± 98.40	312.57 ± 97.73	0.059	0.943
ROM	88.33 ± 17.14	98.63 ± 9.68	104.43 ± 11.57	2.967	0.073
WOMAC scores					
Pain	9.78 ± 1.30	9.63 ± 3.07	6.86 ± 4.00	2.376	0.117
Stiffness	3.22 ± 1.30	2.88 ± 1.46	2.71 ± 1.60	0.263	0.771
Physical function	32.78 ± 4.60	32.38 ± 7.84	29.14 ± 11.28	0.459	0.638
Total WOMAC score	45.78 ± 6.76	44.88 ± 11.96	38.71 ± 15.37	0.837	0.447

Abbreviations: TENS, transcutaneous electrical nerve stimulation; IST, intrasound therapy; 6-MWT, 6-minute walk test; ROM, goniometric measurement of the knee range of motion; WOMAC, Western Ontario and McMaster Universities Arthritis Index.

Table 2. Analysis of clinical outcome measures of patients in the three groups, pre- and postintervention.

VARIABLES	PRIMARY OUTCOME SCORE (WOMAC)				SECONDARY OUTCOME SCORE	
	PAIN MEAN ± SD	STIFFNESS MEAN ± SD	PHYSICAL FUNCTION MEAN ± SD	TOTAL MEAN ± SD	6-MWT (METERS) MEAN ± SD	ROM (°) MEAN ± SD
IST group						
Pre-treatment	9.78 ± 1.30	3.22 ± 1.30	32.78 ± 4.60	45.78 ± 6.76	297.50 ± 67.04	88.33 ± 17.14
Post-treatment	5.44 ± 1.67	1.72 ± 0.22	20.67 ± 4.27	27.89 ± 5.16	322.22 ± 81.76	102.67 ± 11.00
t-value	6.500	2.871	6.154	6.266	–2.528	–2.516
P-value	<0.001*	0.021*	<0.001*	<0.001*	0.035*	0.036*
TENS group						
Pre- treatment	9.63 ± 3.07	2.88 ± 1.46	32.38 ± 7.84	44.88 ± 11.96	302.50 ± 98.40	98.63 ± 9.68
Post-treatment	6.25 ± 2.87	1.63 ± 1.06	21.25 ± 7.40	29.13 ± 10.83	304.54 ± 89.80	102.88 ± 8.18
t-value	3.507	3.416	6.058	5.405	–0.299	–3.126
P-value	0.010*	0.011*	0.001*	0.001*	0.774	0.017*
Exercise only						
Pre-treatment	6.86 ± 4.06	2.71 ± 1.60	29.14 ± 111	38.71 ± 15.37	312.57 ± 97.73	104.43 ± 11
Post-treatment	2.00 ± 1.30	0.29 ± 0.49	11.43 ± 5.35	13.71 ± 6.68	348.14 ± 86.54	107.00 ± 11.1
t-value	3.793	3.545	4.081	4.361	–2.457	–1̃821
P-value	0.009*	0.012*	0.006*	0.005*	0.049*	0.118

Note: *Significant at $P < 0.05$ within the treatment group.
Abbreviations: TENS, transcutaneous electrical nerve stimulation; IST, intrasound therapy; ROM, goniometric measurement of the left knee range of motion; 6-MWT, 6-minute walk test; WOMAC, Western Ontario and McMaster Universities Arthritis Index.

study is imperative because advertisements on the acclaimed benefits of IST in treating a variety of conditions had actually been challenged as misleading, probably because of a lack of scientific basis for this claim.[21]

The aim of this study was to determine if IST would be effective in ameliorating the symptoms of knee OA and thus be an effective, simple, and easy-to-operate treatment option to consider. This is because as enumerated earlier, the simplicity of operation of the intrasound device would minimize the complicated choices of treatment parameters associated with other electrotherapeutic modalities such as TUS.[17] There are, however, conflicting reports on the efficacy of TUS due to the wide variables in technical parameters, such as intensity, duty cycle, frequency, and duration of treatment. Aside from the cost-effectiveness, the only treatment parameter for IST is the intensity of the intrasound device, which is adjusted simply by turning the radial knob anticlockwise.

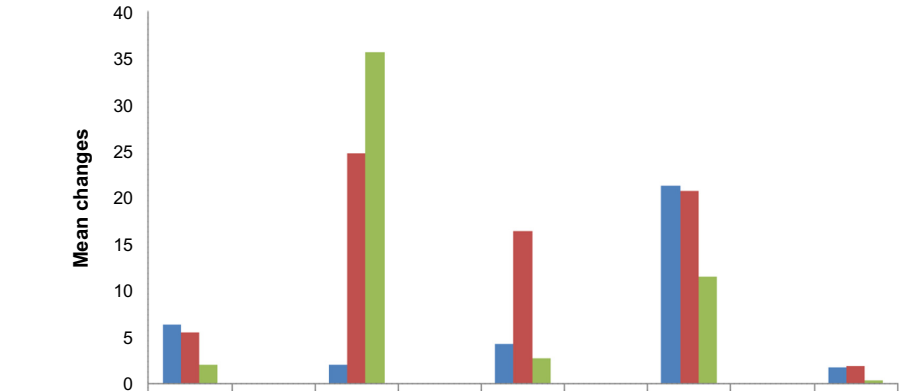
The results show no significant differences in the baseline characteristics of the patients in the three groups except in the age differences that we report as a possible bias (Table 1). There were improvements in clinical outcomes with TENS, IST, and exercises in the patients (Table 2). All primary (WOMAC index) outcome measures improved significantly postintervention in all the groups. However, TENS had no significant impact on the 6-MWT, while the group that had kinematic exercises had no significant improvement in the ROM. This corroborates the report of Roddy et al.[22], which reviewed 19 randomized clinical trials and concluded that both strengthening and aerobic exercises performed on land could reduce pain and improve the function and health status in patients with knee and hip OA compared with education or nonsteroidal anti-inflammatory drugs alone. This study is also in synchrony with a study carried out by Gbiri et al.[23], where it was shown that closed-chain kinematics improve functional performance and reduce symptoms and severity in individuals with knee OA.

There were appreciable differences in the clinical outcome measures for the group that received TENS and exercises when compared with the control group though the latter showed a better improvement in the 6-MWT compared with the former (Fig. 2). This is in conformity with prior studies, which suggested that TENS is effective in reducing pain and improving the WOMAC score but not effective in increasing the 6-MWT performance.[24]

The therapeutic benefits of TENS in improving clinical outcomes could be attributed to its ability to excite the sensory nerves and thereby stimulate the pain gate mechanism and/or the body's opioid system (the body's own pain relieving mechanism),[25,26] thereby rendering the subject pain free for the duration of the exercise.

The group treated with IST and exercises showed an improvement in the clinical outcome measures (WOMAC index, ROM) when compared with those in the control group (Fig. 2). However, kinematic exercises appear to have the best effect in functional improvement in the 6-MWT.

The results as shown in Table 3 showed no significant differences in the outcome measures between IST and TENS as evaluated by the WOMAC scores possibly due to the small



	Pain	6MWT	ROM	P/F	Stiffness
TENS	6.25	2	4.25	21.25	1.63
IST	5.44	24.72	16.33	20.67	1.78
Control	2	35.57	2.71	11.43	0.29

Figure 2. Mean changes in the WOMAC and functional variables pre- and posttreatment across the groups.
Abbreviations: TENS, transcutaneous electrical nerve stimulation; ROM, goniometric measurement of the knee range of motion; 6-MWT, 6-minute walk test; P/F, physical function; IST, intrasound therapy.

sample size of this study. However, as seen in Figure 2, IST had a better clinical effect on the functional outcomes as seen in the mean changes in ROM and 6-MWT. This suggests that while both are effective in ameliorating the symptoms of OA knee, IST could be a better alternative to TENS in view of its more significant effects at improving function, its cost-effectiveness, durability, and simplicity of operation.

In addition to these, studies have shown that IST has the potential benefit of improving healing as shown by the results of prior studies on IST in animal models,[27] which suggested that it improves healing at the cellular level[15] by stimulating the natural healing process of the body[28] in contrast to TENS that acts on sensory nerves to dampen the perception of pain and release the body's natural opioids. This is particularly important especially as Barker and Meletis[29] had suggested that the first intervention in pain management should involve setting a course for healing the tissues that are the source of the pain. In addition to stimulating healing, prior experimental studies also suggested that IST lowered the oxidative stress when given on alternate days following an acute tendon injury in rats.[15,27] The result of this study may substantiate the claims that IST helps by reviving and supporting the self-healing power of the body through gentle improvement of tissue nutrition at a cellular level.[17]

In this study, though treatment with IST was given twice weekly, there was an appreciable improvement in the primary and secondary outcome measures. A study by Aiyegbusi et al.[16] suggested that twice daily treatment was more effective in augmenting healing than once daily treatment. Further studies are needed to determine if a once daily or twice daily treatment with IST would have an even better effect on the clinical and functional outcome measures.

This being a preliminary study, the sample size was small; hence, caution should be exercised in the interpretation of the outcome of this study. Further studies are recommended with a larger sample size that involves a multicentered clinical trial. The sample size for further studies was calculated based on a previous study by Tubach et al.[30], which gave a minimum

Table 3. Post hoc analysis of changes in clinical outcomes measures between IST and TENS.

	IST MEAN ± SEM	TENS MEAN ± SEM	*P*-VALUE
6-MWT	24.72 ± 9.78	2.04 ± 6.82	0.906
ROM	16.33 ± 5.36	7.13 ± 1.76	0.213
WOMAC scores			
Pain	5.44 ± 0.56	6.25 ± 1.01	0.706
Stiffness	1.78 ± 0.22	1.63 ± 0.38	0.915
Physical function	20.67 ± 1.42	21.25 ± 2.62	0.997
Total WOMAC Score	28.0 ± 1.72	29.13 ± 3.83	0.944

Abbreviations: IST, intrasound therapy; TENS, transcutaneous electrical nerve stimulation; ROM, goniometric measurement of the knee range of motion; 6-MWT, 6-minute walk test; WOMAC, Western Ontario and McMaster Universities Arthritis Index.

sample size for each group as 67, and thus, a total of 201 participants will be required for the study.

Strength of the Study

This is, to the best of our knowledge, the first clinical trial on the efficacy of IST as well as the first clinical comparative study of its efficacy with other proven therapeutic modalities.

Conclusion

The results of this study suggest that IST may be an alternative to TENS as an adjunct therapy in the management of OA knee.

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Author Contributions

Conceived and designed the experiments: A Aiyegbusi, OF. Analyzed the data: A Akinfeleye. Wrote the first draft of the manuscript: MA. Contributed to the writing of the manuscript: A Aiyegbusi. Agreed with manuscript results and conclusions: A Aiyegbusi, UO, MA. Jointly developed the structure and arguments for the paper: A Aiyegbusi, UO, MA, OF. Made critical revisions and approved the final version: A Aiyegbusi, UO. All the authors reviewed and approved the final manuscript.

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