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Original Article

Phonophoresis treatment of subacromial impingement syndrome: Pulsed or continuous: A randomized-controlled clinical trial

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ABSTRACT

Objectives: This study aims to compare the effectiveness of pulsed and continuous modes of therapeutic ultrasound (US) for phonophoresis in the treatment of subacromial impingement syndrome (SAIS).

Patients and methods: Between April 2019 and January 2021, a total of 66 patients with SAIS (17 males, 49 females; mean age: 48.2±8.6 years; range, 19 to 64 years) were included. The patients were randomized to the phonophoresis with continuous mode group (n=22), phonophoresis with pulsed mode group (n=22), and phonophoresis with sham US group (n=22). Five grams of ibuprofen phonophoresis was applied in five sessions per week for three weeks for all groups. Primary outcomes were pain intensity as assessed by the Visual Analog Scale (VAS) and shoulder functions by the short version of Disabilities of the Arm, Shoulder and Hand Questionnaire (QuickDASH). The secondary outcome was the quality of life as assessed by the Nottingham Health Profile (NHP). All patients were evaluated at pre-treatment, post-treatment, and at three months after the end of the treatment.

Results: There was a significant improvement in pain during activity, shoulder function, and quality of life after treatment in phonophoresis with continuous and pulsed modes compared to phonophoresis with sham US ($p<0.05$). Phonophoresis with continuous mode was superior to other groups in reducing pain at rest ($p<0.05$). Changes between pre-treatment and the three-month follow-up showed a significant improvement in pain during activity and shoulder functions in phonophoresis with continuous and pulsed modes, compared to phonophoresis with sham US ($p<0.05$). Phonophoresis with pulsed mode was more effective than the other interventions in improving quality of life during the same period ($p<0.05$).

Conclusion: Despite a significant change in phonophoresis with continuous and pulsed modes, it is more pronounced for rest pain in the early period in continuous mode and for quality of life during follow-up in pulsed mode.

Keywords: Continuous mode, phonophoresis, pulsed mode, subacromial impingement syndrome.

Subacromial impingement syndrome (SAIS) is the most frequent complaint of shoulder pain caused by the compression of the supraspinatus tendon between the humeral head and coracoacromial arcus.[1] Its clinical presentation widely varies from bursitis to complete thickness rotator cuff rupture.[2] It is associated with the impaired quality of life with limitation of range of motion of the joint and nocturnal pain, particularly in the advanced stage.

The initial treatment of SAIS is conservative and includes analgesic drugs, steroid injections, and physiotherapy methods.[3] Although the results of previous studies are contradictory, it is usually accepted that exercise, non-steroidal anti-inflammatory drugs,

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and subacromial injections are beneficial.[4,5] To date, many physical therapy modalities have been studied in the literature including extracorporeal shock wave therapy,[6] laser,[1] interferential light therapy,[7] and manual therapy.[8] However, no consensus has been reached upon the most optimal method for the management of SAIS.

Phonophoresis is one of the physiotherapy interventions used for the management of SAIS. It is a way of entering medicine from healthy skin into tissue by the use of therapeutic ultrasound (US). It is a non-invasive method showing positive benefits, particularly with fewer adverse events than the application of drugs by oral or parenteral forms.[9] Therapeutic US has two primary modes: pulsed and continuous. Continuous US modality has a thermal impact, whereas pulsed US provides a mechanical impact such as cavitation, acoustical streaming, micro streaming, increased skin pore area and count, and intercellular place.[10] There are a few studies in the literature comparing these two modes of therapeutic US in phonophoresis. Some authors have suggested that both modes are suitable and effective for the treatment of musculoskeletal disorders.[10,11]

In the present study, we aimed to compare the effectiveness of pulsed and continuous modes of therapeutic US for phonophoresis in the treatment of SAIS.

PATIENTS AND METHODS

This single-center, double-blind, randomized-controlled study was conducted at Çukurova University Faculty of Medicine, Department of Physical Medicine and Rehabilitation between April 2019 and January 2021. Patients with SAIS who were admitted to our patient clinic throughout the study period were screened. Inclusion criteria were as follows: age between 18 and 65 years; having a diagnosis of SAIS with a positive Neer, Hawkins-Kennedy, and empty can tests and magnetic resonance imaging findings compatible with Stage I-II according to the Neer classification; the presence of localized shoulder pain for at least one month; and a Visual Analog Scale (VAS) score of >40 mm. Exclusion criteria were as follows: complete rupture of the supraspinatus tendon; major trauma to the shoulder; diabetes mellitus, hypothyroidism, calcific tendinitis or adhesive capsulitis; cardiac pacemaker; physical therapy for shoulder pain and local cor-ticosteroid injections during the previous six months; and serious cervical spinal pathology. Finally, of 88 patients screened initially, 66 (17 males, 49 females; mean age: 48.2±8.6 years; range, 19 to 64 years) who met the inclusion criteria were recruited. The study flowchart is shown in Figure 1.

Data collection, randomization, and blinding

The patients underwent a detailed history and systemic physical examination, including musculoskeletal and neurological assessments. Baseline laboratory tests were performed to rule out possible etiologies with similar symptoms. Data were collected from the eligible patients by the researcher who was blinded to the study groups. Randomization was performed using computer-generated (R software version 4.2.0) with random permuted blocks of 11 that are six in size by a statistician who was not involved in data collection or statistical analysis. The patients were randomized to the phonophoresis with continuous mode group (n=22), phonophoresis with pulsed mode group (n=22), and phonophoresis with sham US group (n=22). The assignments were stored in numbered sealed envelopes and opened by the physiotherapist who carried out the interventions. The allocation was concealed from the researcher and participants throughout the study.

Interventions

Due to the technical features of the therapeutic US device (Intelect® Mobile, Model 2776; Chattanooga, TN, USA), the frequency of therapeutic US was 1 MHz, with an effective radiation area of 5 cm2 and an intensity of 1 W/cm^2. The US head was used with perpendicular contact for 5 min.

In phonophoresis with continuous mode, the parameters of therapeutic US and treatment procedure were as described above and applied with ibuprofen cream (Ibuactive®; Pharmactive, Tekirdag, Istanbul). The mode of this procedure was continuous (1:1 continuous output). In phonophoresis with pulsed mode, phonophoresis was applied with the same parameters of phonophoresis with continuous mode with ibuprofen cream in pulsed mode (1:4 pulsed output). Five grams of ibuprofen cream was applied for phonophoresis in both modes after stirring with aqua gel. A total of 1 g of ibuprofen cream contains 50 mg of active ingredient. In phonophoresis with sham therapeutic US, the treatment method was as explained for phonophoresis with continuous mode, with the exception that the US device was not initiated.

All participants completed five sessions per week for three weeks (total 15 sessions). In addition, an exercise program including shoulder pendulum exercises,

posterior capsule stretching, range of motion, and isometric shoulder exercises was carried out by a single therapist after each session. This exercise program was recommended to be done at home with 10 repetitions once a day for three weeks. All patients were allowed to use up to 1.000 mg of paracetamol per day as needed.

Outcome measures

The participants were assessed at pre-treatment (baseline), post-treatment, and at three months after the end of the treatment. The primary outcomes of the study were pain intensity as assessed by 100-mm VAS (0 no pain and 100 worst pain)[12] and physical functioning as assessed by the short version of Disabilities of the Shoulder, Arm and Hand Questionnaire (QuickDASH). The latter assesses physical functioning and symptoms of the upper limb, yielding a result between 0 and 100% (0% being the best and 100% being the worst outcomes).[13]

The secondary outcome of the present study was the quality of life as evaluated by the Nottingham Health Profile (NHP). It is a patient-reported

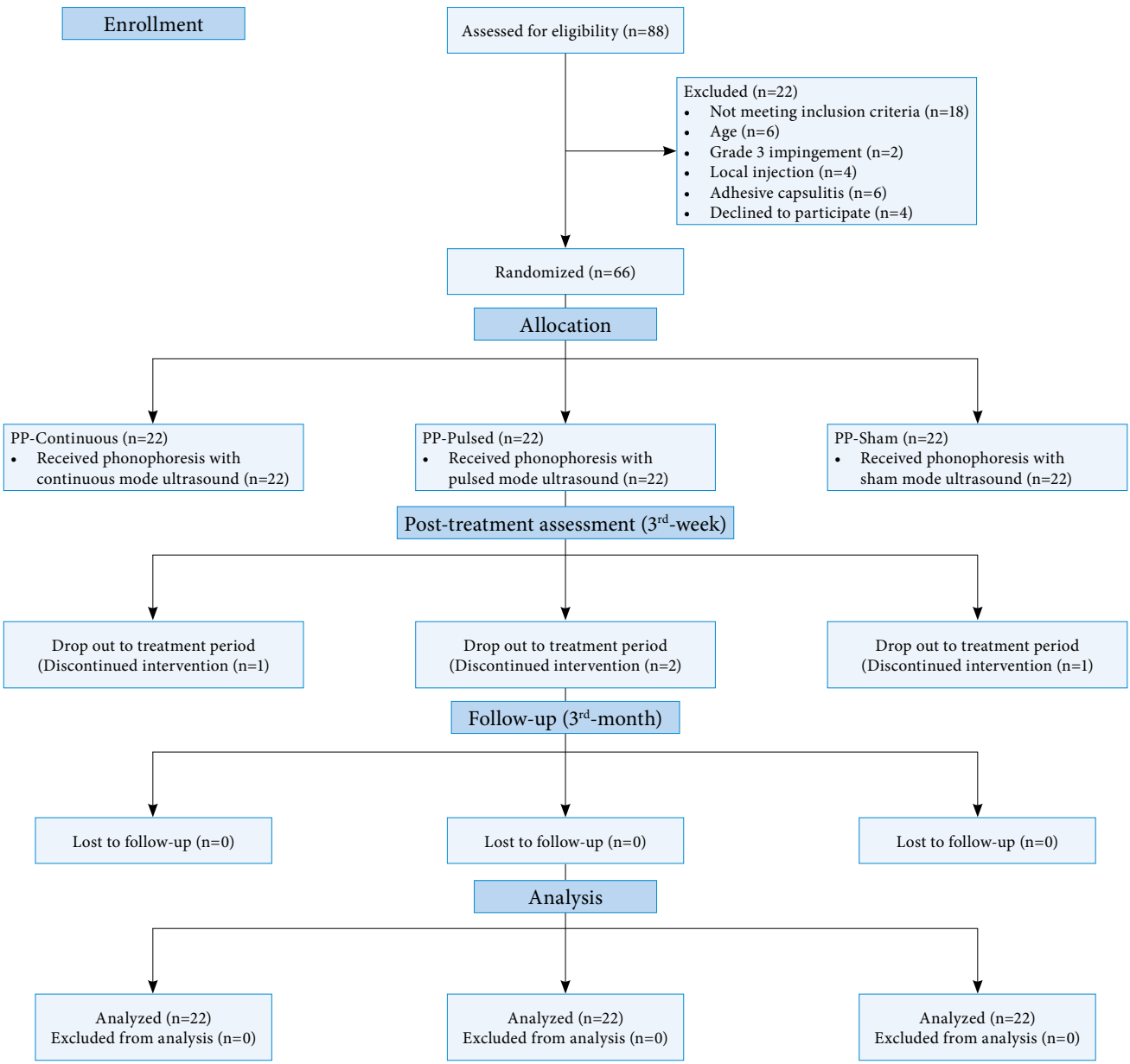

Figure 1. Study flowchart.

PP-Continuous: Phonophoresis with continuous mode; PP-Pulsed: Phonophoresis with pulsed mode; PP-Sham: Phonophoresis with sham ultrasound.

questionnaire that assesses quality of life according to six subscales: pain, sleep, physical mobility, energy level, emotional reaction, and social isolation. The scores range between 0 and 100, and lower scores indicate an improved quality of life.[14]

Statistical analysis

Study power and sample size calculation were performed using the G*Power version 3.0.18 software (Heinrich Heine Universität Düsseldorf, Düsseldorf, Germany). The effect size for the VAS based on the analysis of variance (ANOVA) was considered at 0.25. The correlation between repeated measurements was calculated as 0.5. Considering three measures among the three treatment groups, the sphericity correction was found to be 1.0. We estimated a sample size of 54 participants with a statistical power of 0.95 and a level of 0.05. Considering a possible dropout of up to 20%, a total of 66 patients (n=22 in each group) with SAIS were recruited. An intention-to-treat analysis was carried out and the last available measurement was employed, when the data were missing due to dropouts.

Statistical analysis was performed using the IBM SPSS for Windows version 22.0 software (IBM Corp. Armonk, NY, USA). Visual methods (histograms, probability plots) and Kolmogorov-Smirnov test were performed to test normality of data. Descriptive data were expressed in mean ± standard deviation (SD), median (min-max) or number or frequency, where applicable. The chi-square test and one-way ANOVA were used to compare demographic data among the three study groups at baseline. To analyze intra-group changes and inter-group differences, two-way repeated measures of ANOVA test along with the Bonferroni *post-hoc* test as the adjustment procedure were applied. A *p* value of <0.05 was considered statistically significant.

RESULTS

There was a high degree of compliance (only one in phonophoresis with continuous mode, two in phonophoresis with pulsed mode, and one in phonophoresis with sham therapeutic US discontinued interventions) to all three interventions (Figure 1). No adverse effects were observed.

There were no significant differences among the groups in terms of the demographic data (p>0.05 for all), except for age (p=0.020) and number of patients receiving paracetamol (p=0.215) (Table 1). Age was not found to be a significant covariate for pain or function, nor was it a significant predictor of follow-up scores (p>0.05).

The analysis of variance showed a significant effect for group×time in VAS (p=0.001 for activity pain and p=0.017 for pain at rest), QuickDASH (p<0.001), NHP-pain (p=0.011), NHP-energy level (p=0.022), and NHP-physical mobility (p=0.017). However, there was no significant group×time effect for NHP-sleep (p=0.191), NHP-emotional reactions (p=0.218), and NHP-social isolation (p=0.207).

The intra-group analysis demonstrated a significant difference between the three assessments regarding VAS, QuickDASH, and NHP (except for NHP-sleep and NHP-energy levels) in all groups (p<0.017 for all). *Post-hoc* analyses carried out for pairwise comparisons showed a significant improvement in outcome measures (except for NHP-sleep and NHP-energy level) with respect to time in all groups (Table 2).

TABLE 1
Demographic and clinical characteristics of the patients

	PP-Continuous (n=22)			PP-Pulsed (n=22)			PP-Sham (n=22)			
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			44.8±6.9			50.7±8.8			49.1±9.2	**0.020***
Sex										0.917
Male	6	27		5	23		6	27		
Female	16	73		17	77		16	73		
Affected shoulder										0.783
Right	13	59		15	68		13	59		
Left	9	41		7	32		9	41		
Symptom duration (month)			7.3±2.7			6.4±3.4			7.2±3.6	0.354
Number of patients used paracetamol	12	55		10	45		13	59		0.215

PP-Continuous: Phonophoresis with continuous mode; PP-Pulsed: Phonophoresis with pulsed mode; PP-Sham: Phonophoresis with sham ultrasound; SD: Standard deviation;
* Pairwise comparisons for PP-Continuous-PP-Pulsed at a significance level of <0.05.

The changes between pre- and post-treatment assessments revealed that phonophoresis with continuous mode was superior to phonophoresis with pulsed mode and phonophoresis with sham therapeutic US in reducing pain at rest (p=0.025 and p=0.002, respectively). However, phonophoresis with continuous mode and phonophoresis with pulsed mode showed a significant difference in improving pain during activity (p=0.001 and p=0.044, respectively) and shoulder functions (p=0.046 and p=0.001, respectively), compared to phonophoresis with sham therapeutic US. Considering the quality

TABLE 2
Intra-group comparisons of the outcome measures at pre-treatment (t0), post-treatment (t1), and at three months of follow-up (t2)

	Pre-treatment (t0)	Post-treatment (t1)	Follow-up (t2)				
Groups	Mean±SD	Mean±SD	Mean±SD	$p^{t0\text{-}t1\text{-}t2}$	$p^{t0\text{-}t1}$	$p^{t0\text{-}t2}$	$p^{t1\text{-}t2}$
VAS (mm) rest							
PP-Continuous	21.3±10.3	7.4±7.1	6.8±7.1	**<0.001**	**<0.001**	**<0.001**	0.519
PP-Pulsed	19.9±15.9	8.9±11.2	6.1±7.1	**<0.001**	**<0.001**	**<0.001**	0.059
PP-Sham	20.6±11.5	3.6±9.7	11.1±9.5	**<0.001**	**<0.001**	**<0.001**	**0.001**
VAS (mm) activity							
PP-Continuous	60.8±16.2	22.4±13.7	19.1±13.0	**<0.001**	**<0.001**	**<0.001**	**0.001**
PP-Pulsed	54.6±12.0	24.6±15.1	17.4±12.2	**<0.001**	**<0.001**	**<0.001**	**0.004**
PP-Sham	54.9±13.6	34.8±14.8	27.7±14.3	**<0.001**	**<0.001**	**<0.001**	**<0.001**
QuickDASH							
PP-Continuous	56.9±11.8	34.8±13.6	31.9±14.0	**<0.001**	**<0.001**	**<0.001**	**<0.001**
PP-Pulsed	52.1±8.1	25.1±9.9	19.9±10.4	**<0.001**	**<0.001**	**<0.001**	**0.002**
PP-Sham	49.6±7.6	34.2±15.2	32.3±16.1	**<0.001**	**<0.001**	**<0.001**	0.184
NHP pain							
PP-Continuous	39.2±10.8	24.2±14.3	20.8±14.8	**<0.001**	**<0.001**	**<0.001**	**0.011**
PP-Pulsed	53.2±26.1	30.6±25.6	23.8±20.2	**<0.001**	**<0.001**	**<0.001**	0.037
PP-Sham	54.6±20.1	44.9±19.1	34.7±22.1	**<0.001**	**0.001**	**<0.001**	**0.003**
NHP sleep							
PP-Continuous	14.7±14.8	9.3±11.4	6.0±10.7	**<0.001**	**<0.001**	**<0.001**	0.025
PP-Pulsed	21.9±25.5	17.4±20.5	14.2±19.5	**0.001**	0.340	**0.004**	0.025
PP-Sham	22.2±21.0	23.7±26.0	19.2±23.8	0.086	0.480	0.248	0.058
NHP energy level							
PP-Continuous	14.4±6.8	9.6±5.1	7.4±3.8	**0.004**	0.034	**0.011**	0.157
PP-Pulsed	45.1±29.9	36.5±13.7	25.8±16.8	**<0.001**	**<0.001**	**<0.001**	**0.004**
PP-Sham	32.5±23.6	29.2±10.7	25.9±10.2	0.082	0.136	0.089	0.063
NHP emotional reactions							
PP-Continuous	17.0±7.3	13.3±6.4	9.6±5.0	**<0.001**	**<0.001**	**<0.001**	**0.008**
PP-Pulsed	24.7±9.8	16.1±8.8	12.1±11.9	**<0.001**	**<0.001**	**<0.001**	0.400
PP-Sham	24.4±13.7	19.3±12.1	15.6±13.3	**<0.001**	**<0.001**	**<0.001**	0.035
NHP social isolation							
PP-Continuous	8.7±3.6	5.3±5.0	3.3±3.6	**<0.001**	**<0.001**	**<0.001**	**0.008**
PP-Pulsed	4.5±3.4	4.5±4.3	3.9±3.1	**<0.001**	**<0.001**	**<0.001**	0.400
PP-Sham	9.9±8.4	5.2±4.2	6.7±5.5	**<0.001**	**<0.001**	**<0.001**	0.035
NHP physical mobility							
PP-Continuous	27.5±10.1	15.4±8.4	13.3±2.7	**<0.001**	**<0.001**	**<0.001**	0.025
PP-Pulsed	37.9±16.9	26.2±9.7	21.8±8.0	**<0.001**	**<0.001**	**<0.001**	0.147
PP-Sham	38.4±16.6	33.3±17.7	26.8±8.9	**<0.001**	**0.011**	**<0.001**	0.019

PP-Continuous: Phonophoresis with continuous mode; PP-Pulsed: Phonophoresis with pulsed mode; PP-Sham: Phonophoresis with sham ultrasound; SD: Standard deviation; VAS: Visual Analog Scale; QuickDASH: Short version of Disabilities of the Arm, Shoulder and Hand Questionnaire, NHP: Nottingham Health Profile.

TABLE 3
Inter-group comparison of the changes for outcome measurements

Outcomes	PP-Continuous minus PP-Pulsed						PP-Continuous minus PP-Sham						PP-Pulsed minus PP-Sham					
	Difference of the changes						Difference of the changes						Difference of the changes					
	Post-intervention			3rd-month follow-up			Post-intervention			3rd-month follow-up			Post-intervention			3rd-month follow-up		
	Mean	95% CI	Effect size (d)	Mean	95% CI	Effect size (d)	Mean	95% CI	Effect size (d)	Mean	95% CI	Effect size (d)	Mean	95% CI	Effect size (d)	Mean	95% CI	Effect size (d)
VAS-Rest	-2.9*	-5.2/-0.6	0.37	0.7	-7.9/6.5		-6.9*	-13.4/-0.4	0.94	-5.0	-12.5/2.5		-4.1	-10.6/2.4		-4.3	-11.7/3.1	
VAS-Activity	-8.4	-18.6/ 1.8		-4.5	-14.8/ 5.8		-18.3*	-28.9/-7.7	1.14	-14.5*	-25.1/-3.8	0.80	-9.9*	-19.7/-0.1	0.67	-10.0*	-19.4/-0.6	0.62
QuickDASH	4.9	-3.0/12.8		7.1	-1.2/ 15.4		-6.6*	-11.7/-1.5	0.49	-7.7*	-14.5/-0.9	0.54	-11.5*	-19.5/-3.5	1.17	-14.8*	-23.3/-6.3	1.05
NHP-Pain	7.6	-3.0/14.2		11.1*	0.4/21.8	0.54	-5.3*	-7.3/-3.3	0.50	1.6	-9.5/12.7		-12.9*	-21.4/-4.4	0.76	-9.5*	-18.6/-0.4	0.58
NHP-EL	3.8	-6.3/13.8		12.3*	0.9/ 23.7	0.67	-1.5	-11.9/8.9		-0.4	-12.3/11.4		-5.3	-15.6/5.0		-12.7*	-24.4/-1.0	0.61
NHP-PM	-0.4	-7.0/ 6.2		2.0	-6.2/10.2		-7.0*	-13.8/-0.2	0.69	-2.6	-11.1/5.9		-6.6*	-13.0/-0.2	0.39	-4.6	-13.0/3.9	

PP-Continuous: Phonophoresis with continuous mode; PP-Pulsed: Phonophoresis with pulsed mode; PP-Sham: Phonophoresis with sham ultrasound; VAS: Visual Analog Scale; QuickDASH: Short version of Disabilities of the Arm, Shoulder and Hand Questionnaire; NHP: Nottingham Health Profile; EL: Energy level; PM: Physical mobility; * p<0.05.

of life of the patients, no significant differences were observed between interventions for sleep, energy level, emotional reaction and social isolation parameters (p>0.05 for all). However, phonophoresis with continuous mode and phonophoresis with pulsed mode were more effective in improving NHP-pain (p=0.042 and p=0.006, respectively) and physical mobility parameters (p=0.026 and p=0.038, respectively), compared to phonophoresis with sham therapeutic US (Table 3).

The changes between the three-month follow-up and baseline assessments demonstrated that, unlike the post-treatment period, there was no significant difference between interventions in reducing pain at rest (p>0.05). However, similar to the post-treatment period, phonophoresis with continuous mode and phonophoresis with pulsed mode were superior to phonophoresis with sham therapeutic US for improving pain during activity (p=0.006 and p=0.035, respectively) and shoulder functions (p=0.043 and p=0.001, respectively). Furthermore, for NHP-pain and energy level parameters, phonophoresis with pulsed mode showed a significant improvement compared to phonophoresis with continuous mode (p=0.018 and p=0.023, respectively) and phonophoresis with sham therapeutic US (p=0.043 and p=0.012, respectively). There was no significant difference between interventions for sleep, emotional reaction, social isolation, and physical mobility parameters (p>0.05 for all) (Table 3).

DISCUSSION

In the present study, we examined whether pulsed or continuous modes of therapeutic US were effective in phonophoresis treatment. Our study results showed that pulsed and continuous phonophoresis combined with exercise were more effective than phonophoresis with sham US plus exercise in decreasing pain and enhancing shoulder functions in patients with SAIS. Although there was a significant change in both modes, the continuous mode yielded more favorable results in reducing pain at rest than the pulsed mode in the early period. However, the pulsed mode was more effective than the continuous mode for improving quality of life at the three-month follow-up.

Phonophoresis has been used in many musculoskeletal diseases and has been reported to be successful in the management of SAIS,[3,15] lateral epicondylosis,[16] low back pain,[17] carpal tunnel syndrome,[18] knee osteoarthritis,[19,20] and

temporomandibular disorders.[21] However, there is a limited number of studies comparing pulsed versus continuous mode phonophoresis, and most of them have been conducted in *in vitro* settings.[10,22,23] In a study, Ebrahimi et al.[10] compared these two modes of therapeutic US and assessed the effect of lidocaine phonophoresis on absorption and sensory blockade. The authors reported that the absorption was significant for both modes of US. However, the effect was more prominent in the pulsed mode. Unlike this study, in our study, we found that both modes were effective; however, the continuous mode seemed to be more effective after the treatment. The discrepancy between the studies can be attributed to the drug used. In an *in vitro* study by Yang et al.,[23] the highest permeability was achieved in low frequency and continuous mode. In another study in which ibuprofen was also used as an active ingredient, permeability was better in the continuous mode.[22] These findings are consistent with our results.

Although there are very few head-to-head studies comparing these two modes, there are several studies using a single mode. Some authors have suggested that the continuous mode is therapeutically effective,[15,17,19] while others have proposed that the pulsed mode is effective.[24] For the drug applied in phonophoresis to be effective, the permeability must be increased permanently or temporarily along the corneocytes and keratinocytes, probably due to thermal effects and mechanical stress.[25] The thermal effects of the continuous mode cause augmented fluidity of intercellular lipids and enlargement of intercellular spaces. Additionally, this effect of the continuous mode may disturb the drug molecules in superficial blood vessels.[25] Advocates of this view point out that the continuous mode provides greater drug penetration, but other effects in the pulsed mode are not sufficient for this condition.[11] The pulsed mode has mechanical effects such as cavitation, acoustic streaming, and microstreaming.[10] It is also well documented that the cavitation effect (i.e., formation of air bubbles within keratinocytes) of the pulsed mode causes transient hyperthermia. However, it is considered that this situation is not relevant. The oscillation of small cavitation bubbles produces mechanical stress in the blood vessels, thereby increasing skin porosity and drug penetration due to the cavitation effect.[10,26] We believe that the mechanisms of both pulsed and continuous modes may be effective in drug permeability. In this case, it may be the drug type and other parameters of US that would make a difference in permeability.

The primary outcome measures of the present study were VAS and QuickDASH scores. The VAS is widely used in the evaluation of musculoskeletal pain in clinical trials. In a study by Tashjian et al.,[27] the minimal clinically important difference (MCID) value was estimated to be 1.4 cm for rotator cuff diseases on a 10-cm VAS measuring pain.[27] In our study, more than MCID values were obtained during the early post-treatment period in all groups during activity. This improvement was more pronounced in phonophoresis with continuous mode than in the other groups. This improvement was maintained during the follow-up period. For pain at rest, MCID values were reached only in phonophoresis with continuous mode. Although drug permeability is observed in both modes, the drug permeability in continuous mode may be higher than that in pulsed mode. This can be explained by the thermal effect of the continuous mode, which makes the drug permeability increasingly faster.

In the present study, the QuickDASH was used for the assessment of physical functioning. In a study, the MCID value for moderate improvement in the QuickDASH was calculated as 15.91 points.[28] The MCID score in QuickDASH was achieved in phonophoresis with continuous mode and phonophoresis with pulsed mode immediately after treatment. This situation was maintained during follow-up in both interventions. Furthermore, in general, the necessary values for functional recovery were achieved very easily in phonophoresis with continuous and phonophoresis with pulsed modes. However, the MCID value in QuickDASH in phonophoresis with sham therapeutic US could be reached in the follow-up period. This finding indicates that phonophoresis treatment should be added together with exercise for rapid functional recovery. Although the positive results of exercise therapy are known, it should be kept in mind that its effects begin in a late period. When pain and functional status are evaluated together, both the continuous mode and pulsed mode are effective; however, the continuous mode can be considered primarily in cases where pain at rest is at the forefront.

Nonetheless, there are some limitations to this study. The frequency and intensity of therapeutic US were 1 MHz and 1 W/cm^2, respectively. The parameters used were the most frequent in daily practice. The duration of the US treatment was 5 min. Other frequency and intensity values and treatment durations that are likely to alter treatment outcomes

were not tested. In this study, ibuprofen was used as the active substance, but another active substance (e.g., dexketoprofen, aceclofenac, betamethasone) that can be used may affect the results. Additionally, this study has a relatively short-term follow-up.

In conclusion, our study results show that ibuprofen phonophoresis with both pulsed and continuous modes combined with exercise is more effective than phonophoresis with sham US combined with exercise in reducing pain and improving shoulder functions. The desired therapeutic results can be achieved in the early period in phonophoresis applications, which sustain for up to three months. In our study, we observed a statistically significant difference in the results of the continuous mode for pain at rest and during activity in the early period and pulsed mode for pain during activity and shoulder functions during follow-up. These results may provide early clinical improvement, as well as return to work and, thus, less economic loss. Nevertheless, further large-scale, long-term, prospective, randomized-controlled studies are warranted to confirm these findings.

Ethics Committee Approval: The study protocol was approved by the Adana City Training and Research Hospital Local Ethics Committee (date: 16.12.2020, no: 1185). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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