Pulsed Shortwave Therapy in Cervical Osteoarthritis: An NSAID- Controlled, Randomized Clinical Trial

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Abstract

Objective Assess treatment superiority of Pulsed Shortwave Therapy (PSWT) against COX-2 NSAID therapy, in reducing disability and pain due to cervical osteoarthritis.

Design 200chronic pain suffers (average pain duration about 2 years)diagnosed with cervical osteoarthritis by radiological imaging were randomized into one of two treatmentarms: COX-2 NSAID treatment: Etoricoxib 60mg/day for 4 weeks; or, PSWT treatmentworn 24 hours/day for 4 weeks. The primary outcome measure was the 4-week score on the Neck Disability Index (NDI): a 10-question assessment on a 50-point scale. Secondary outcome measures included pain(at rest and during activity)measured on a Visual Analog Scale (VAS)of0-100 mm, dose count of rescue pain medication (paracetamol)use and a treatment satisfaction rating. These 4-week scores were compared across the two arms to assess superiority.

Results After 4 weeks of treatment,subjects in both study arms reported significantly lower ($p<0.0001$) 4-week measures (11.24-NSAID;9.34-PSWT; 0-50 points),VAS_{rest} (30.08-NSAID;22.76-PSWT; 0-100 mm) and $VAS_{activity}$ (36.40-NSAID; 27.42-PSWT; 0-100 mm).The absolute reduction from baseline in NDI was significantly greater in the PSWT arm than NSAID arm(by 3.66 points; 95% CI 2.3 to 5.02; $p<0.0001$). Similarly, the reductions from baseline inVAS_{rest} and $VAS_{activity}$were significantly greater in the PSWT arm than NSAID arm(by 10.89 mm;95% CI 6.90 to 14.87; $p<0.0001$ and 12.05 mm;95% CI 7.76 to 16.33; $p<0.0001$ respectively).The PSWT arm used 50% less rescue pain medication. Eleven adverse effects were reported in the NSAID arm and zero in the PSWT arm.

Conclusion Both NSAID and PSWT treatments resulted in clinically meaningful increases in quality of life(NDI) and decreases in pain (VAS) associated with cervicalosteoarthritis. However, the PSWT armshowed superior improvements in all outcome measures when compared to the NSAID armwith no adverse effects.

1.0 Introduction

Cervical osteoarthritis (COA), or cervical spondylosis, refers to the degeneration of the joints in the cervical region of the neck commonly arising from dehydrated/herniated vertebrae, bone spurs, and/or stiff ligaments [1]. COA is highly age dependent and is present in all adults over 40 years of age [2]. However, these degenerative changes are only weakly associated with clinical symptoms of chronic pain and stiffness in patients diagnosed with COA by radiographic imaging [3, 4]. A similar weak association between the severity of joint degeneration and intensity of pain has been previously reported for knee osteoarthritis (KOA) [5, 6]. In KOA, hypersensitivity in the surrounding tissues arising through central sensitization is understood to be an important factor in pain generation. Similar logic would imply that central sensitization[7] may be a contributing factor in individuals suffering with COA-related chronic pain.

While surgical interventions are recommended in more advanced stages, first line treatment for COA (< 6 weeks) often involves non-steroidal anti-inflammatory drugs (NSAIDS) and physical therapy [2]. NSAIDS are widely used both as a self-administered over the counter therapy and from prescription to manage pain and inflammation resulting from osteoarthritis (OA). However, there are significant adverse effects associated with chronic use, including gastrointestinal [8] (GI) and cardiovascular complications including myocardial infarction [9–11].

COX-2 specific NSAIDS (Coxibs) were developed to mitigate the incidence of GI complications associated with chronic NSAID use. Coxibs have been shown to be as effective as non-specific NSAIDS, e.g. ibuprofen, ketoprofen, diclofenac [8]. Etoricoxib is a COX-2 specific NSAID that is orally administered [12] and well-established as a therapy for arthritic conditions including osteoarthritis of the knee [13, 14], hip [14] and rheumatoid arthritis [15]. Etoricoxib has also been shown to be an effective analgesic for acute postoperative pain [16], chronic low back pain [17], gout [18], ankylosing spondylitis [19, 20] and other pain conditions [21]. A daily dose of 60 mg Etoricoxib has been established as an effective

therapy for relieving pain due to osteoarthritis [13, 19]. Where currently available Coxibs have been shown to reduce GI associated risks [22], when compared to non-specific NSAIDS; all NSAIDs have a similar risk profile for inducing cardiovascular complications [9–11, 23, 24]. The US Centers For Disease Control (CDC) acknowledges these challenges and recommends that non-pharmacological therapies be utilized as the first line of treatment against chronic pain [25].

Pulsed Shortwave Therapy (PSWT) is a non-invasive therapy which relies on tissue exposure to high-frequency, non-thermal electromagnetic energy [26] with the goal of providing analgesia from acute postoperative pain [27, 28] and chronic pain [29–34]. With regards to osteoarthritis, PSWT has been demonstrated to reduce pain and thereby improve physical functionality and the need for additional pharmacotherapy including NSAIDs [29]. When used as an adjunctive therapy, PWST has also been shown to be effective in reducing pain for a number of chronic conditions within 7 days of initial use [32–34], with durability of treatment extending for at least 6 months[35]. Lack of adverse effects [34] makes PSWT especially attractive for use as a first-line treatment for COA. However, to date no clinical study has investigated the relative effectiveness of PSWT against other first-line treatments such as NSAIDs.

The goal of this study was to investigate the effectiveness of PSWT in improving physical functionality and reducing pain in individuals diagnosed with cervical osteoarthritis in comparison to the effectiveness of NSAIDs. Specifically, we hypothesized that PSWT would provide superior performance when compared to COX-2 NSAIDs in a randomized trial of cervical osteoarthritis patients.

2.0 Methods

This single center, parallel arm, randomized (1:1) trial was designed to test the hypothesis that PSWT is superior to NSAID as a treatment intervention for chronic pain sufferers (≥ 2 months) diagnosed with COA. The study was approved by the ethics review board of New Mazloum Hospital, Tripoli, Lebanon. The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, and relevant Good Clinical Practices (GCP). The study was registered on clinicaltrials.gov (NCT03542955).

2.1 Subjects

Adult men and women who presented at the clinic of the principal investigator and who were suffering neck pain and seeking treatment were eligible for the study. Inclusion criteria for participation in the study were as follows: a) a diagnosis of cervical osteoarthritis using a validated radiological imaging grading system [4], b) COA related pain lasting 2 months or more; and c) no use of prescription analgesics for at least 2 months prior to the study. Subjects who were pregnant, had osteoporosis or any neurological, muscular, hematological, or auto-immune diseases were excluded from the study. The principal investigator fully explained the study to eligible patients including the procedures and the treatment arms; those willing to participate were enrolled into the study after providing written consent. Subjects who declined to be involved continued with treatment under the principal investigator. Once enrolled in the study, home visits were schedule for the first 2 days to validate accurate use of the assigned intervention, followed by weekly in person or by phone contact to determine patient compliance.

2.2 Treatments

The NSAID treatment was 60 mg Etoricoxib tablets (Arcoxia® Merck, Kenilworth, NJ, USA), taken once daily. Arcoxia is available in more than 80 countries worldwide, but not in the US, where the US Food and Drug Administration has required additional safety and clinical testing.

The PSWT treatment was a commercially available device (ActiPatch®, BioElectronics Corporation, Frederick, MD, USA) used 24 hours daily, except when bathing. ActiPatch is a class II device and indicated for over-the-counter treatment of musculoskeletal pain in the US, and general soft-tissue pain in the EU and Canada. The device emits electromagnetic energy at a frequency of 27.12 MHz which is pulsed at 1 kHz with a pulse duration of 100 microseconds. The device has a treatment area of 110 cm^2 and peak incident power density of 73μW/cm^2 (as measured into a 50-ohm load). The device is attached over the location of pain in the cervical region with adhesive tape (Fig. 1). Subjects in both arms were provided with rescue medication (1 g paracetamol), to be taken as needed in 2 × 500 mg tablets, with an advised maximum daily dose of 4 grams.

2.3 Randomization and Treatment Arms

Following enrollment, subjects were taken to a separate examining room and were randomized into one of the two treatment arms in the following manner: two hundred cards, with 100 indicating PSWT treatment and 100 indicating NSAID treatment, were prepared. A designated individual randomly drew a card from a pre-shuffled deck that determined the assignment for each enrolled patient. This card was then discarded. The principal investigator was not involved with subject randomization and was therefore blinded to subject arm allocation.

Outcome Measures

Subjects provided measures at baseline and at the end of the 4-week study period. Initially subjects provided demographic information, i.e., age, gender, height, weight, (from which BMI was calculated) and baseline scores for functionality and pain level. The primary outcome measure was the Neck Disability Index (NDI), a condition-specific, functional status questionnaire with 10 items (pain, personal care, lifting, reading, headaches, concentration, work, driving, sleeping and recreation)[36]. Each item has six possible responses, with a maximum score of 5 (0 being least disabled, 5 being most disabled), resulting in a maximum NDI score of 50 (higher scores indicate less functionality). Scores of 15–24 are classified as being moderately disabled and scores 25–34 are classified as severely disabled. The NDI used in this study was a validated Arabic version [37]. Secondary outcome measures were pain levels at rest and during physical activity (one lateral and medial rotation of the head) were obtained using a 0-100 visual analog scale (VAS). These measures were determined by subjects marking on a 100 mm line anchored by no pain at 0 and excruciating pain at 100 mm. At the end of the 4 weeks subjects again provided information on functionality (via NDI) and pain levels (via VAS). In addition, rescue medication use and treatment satisfaction were assessed.

Statistical Analysis

The size of the population needed to establish superiority in the study was calculated, *a-priori*, by estimating a 5-point difference in average treatment effect score of the primary endpoint (NDI) between the two treatment arms. For a two-tailed test with $\alpha = 0.05$ and $\beta = 0.2$ (80% power), the sample size was calculated to be 172 (86 in each arm). To allow for a 15% dropout rate, the total sample size for the study was set at 200 subjects.

Statistical analyses were performed using Microsoft Excel (*Microsoft Corporation, Redmond, Washington*) and an Excel add-on, Regressit. Analyses to determine if one or both arms provided clinically significant improvement in functionality and pain relief will compare the 4-week measures to the relevant baselines measures using two-sided students *t-tests.* To test for superiority of PSWT compared to NSAIDs 4-week scores for the relevant measures will be compared using two-sided students *t-tests*. If baseline measures differ across the two arms, the difference in absolute reduction in the relative measure will be compared using two-sided students *t-tests* and ANCOVA. Since medication use and treatment satisfaction are assessed only at the end of the study, only the difference across the two arms will be compared using an unpaired *student's t*-test. Analyses will be perform on the intent-to-treat data set and all tests will use $p < .05$ as the threshold for assessing statistical significance level.

Results

A total of 542 subjects were screened for eligibility for the study (Fig. 2) before the enrollment target of 200 eligible subjects was met. Twenty percent of screened subjects (108) declined to participate, while 234 did not meet the inclusion criteria. Of the 200 subjects enrolled in the study, 3 were lost to follow up: 2 in the Etoricoxib arm and 1 in the PSWT arm. These 3 subjects were considered dropouts, but included in the statistical analysis by assuming no changes in any measure (Fig. 2). All remaining (197) subjects were found to be compliant with the assigned treatment regime i.e. regularly taking prescribed dose of Etoricoxib or using the PSWT device continuously except for bathing.

Baseline demographics, COA grade, and baseline scores for NDI index and the two VAS measures are presented in Table 1. On average participants were experiencing neck pain for about 24 months and thus can be classified as chronic pain sufferers. These subjects reported a baseline NDI score of 24.5, indicating borderline severe disability and baseline pain scores during rest and activity exceeding 70 VAS mm, thus classifying them as severe pain sufferers.

Each of the measures was compared across the two arms. There were statistically significant differences across the two arms in age, NDI and the two VAS scores although in the latter three measures these differences were not clinically significant. In each case the PSWT arm reported, on average, less functionality and higher pain levels.

Table 1
Baseline demographic and clinical characteristics of the PSWT and NSAID arms. There were statistically significant differences across the two arms in age, NDI and VAS scores. However, the magnitude of these differences indicates no clinically meaningful differences in composition between the two treatment arms.

Baseline Demographic Data		All Subjects (N = 200) Mean (SD)	PSWT Arm (N = 100) Mean (SD)	NSAID Arm (N = 100) Mean (SD)	*p* value of PSWT Vs NSAID Means
Age (yr)		44.95 (10.3)	46.40 (11.8)	43.47 (8.3)	0.04
Height (cm)		164.9 (7.8)	165.3 (7.9)	164.47 (7.8)	0.45
Weight (Kg)		75.5 (14.8)	76.2 (15.8)	74.7 (13.8)	0.47
BMI		27.61 (4.0)	27.72 (4.2)	27.50 (3.9)	0.7
Disease Duration (months)		24.13 (24.1)	24.4 (23.5)	23.9 (24.8)	0.88
Radiographic Imaging COA Grade		2.69 (0.70)	2.75 (0.73)	2.63 (0.66)	0.22
Gender (%)	Men	28.5%	35%	22%	0.04
	Women	71.5%	65%	78%	0.04
VAS_{rest} (0-100)		70.78 (9.9)	72.57 (10.93)	69 (8.66)	0.01
VAS_{active} (0-100)		78.32 (9.4)	79.95 (10.38)	76.7 (8.15)	0.01
Neck Disability Index (NDI) (0–50)		24.57 (3.0)	25.42 (3.77)	23.66 (2.66)	0.0002

Neck Disability Index (Functionality) and Visual Analog Scale (Pain)

After four weeks of treatment, subjects in both treatment arms reported lower mean scores for NDI, VAS_{rest} and VAS_{active}) and these 4-week scores were statistically significant ($p < .0001$) from the relevant baseline measure (Table 2). The change in each component score is presented in supplemental Fig. 1.

Table 2

Subjects in both treatment arms reported a statistically significant reductions ($p < 0.0001$) in the three outcomes NDI, VAS_{rest} and VAS_{active} when treatment scores were compared to their respective baseline score.

Outcome Measure	PSWT Arm Score Mean (SD)				NSAID Arm Score Mean (SD)			
	Baseline	4-weeks	Mean Difference	P value	Baseline	4-weeks	Mean Difference	P value
NDI	25.42 (3.77)	9.34 (4.46)	16.08 (5.21)	$p < .0001$	23.66 (2.66)	11.24 (4.68)	12.42 (4.54)	$p < .0001$
VAS_{rest}	72.57 (10.93)	22.76 (12.78)	49.81 (15.15)	$p < .0001$	69 (8.66)	30.08 (14.60)	38.92 (13.39)	$p < .0001$
VAS_{active}	79.95 (10.38)	27.42 (14.81)	52.53 (15.92)	$p < .0001$	76.7 (8.15)	36.40 (16.40)	40.3 (14.77)	$p < .0001$

To assess whether PSWT treatment was statistically superior to NSAID, 4 week treatment scores were compared between the two arms. In each of the three cases we find this difference is statistically significant at the $p < 0001$ level with subjects in the PSWT arm reported lower scores (Table 3, Supplemental Fig. 2). We also compared the mean difference in the outcome measures from the respective baseline and find these differences adjusted for baseline scores to be statistically significant at the $p < 0001$ level in favor of the PSWT arm. The standardized effect size was also calculated for the three outcome measures and the results can be seen in (Fig. 3) showing a large and consistent standardized effect size for the PSWT treatment.

Finally, to control for any differences in demographics as well as the baseline relevant outcome measures, we augmented our statistical analyses with ANCOVA analysis using ordinary least square regression and a dummy variable for the two arms. The dependent variables (DV) in these analyses were 4-week scores of the relevant outcome measure. The independent variables included a dummy variable associated with using the device (NSAID = 0; PSWT = 1), subject demographics (age, BMI, gender, duration of pain, OA grade) and the baseline score of relevant outcome measure.

The forecasted mean “adjusted” 4-week scores for the three measures and standard deviations of these adjusted mean are presented in the right hand column of Table 3, again indicating that PSWT treatment resulted in lower 4-week scores (i.e., was superior to NSAID treatment.) In addition this analysis found the coefficients for both BMI and baseline relevant measures (i.e., NDI/VAS) were statistically significant, indicating that subjects with higher BMI and higher baseline NDI/VAS scores reported less treatment efficacy at 4-weeks. No other variables were statistically significant in these analyses.

Table 3

The difference of mean differences between the two treatment arms: 1) as measured; and 2) after adjusting for demographics and baseline scores using ANCOVA. Statistical significance ($p < 0.0001$) was shown in both tests.

Outcome Measure	Measured 4- Week Score Mean (SD)		Comparison of Means (*p value*)	Adjusted (Regression) 4-Week Score Mean (SD)		Comparison of Means (*p value*)
	PSWT	NSAID		PSWT	NSAID	
NDI	9.34 (4.46)	11.24 (4.68)	$p < .0001$	9.00 (4.34)	11.58 (4.34)	$p < .0001$
VAS_{rest}	22.76 (12.78)	30.08 (14.60)	$p < .0001$	21.98 (13.10)	30.84 (13.10)	$p < .0001$
VAS_{active}	27.42 (14.81)	36.40 (16.40)	$p < .0001$	26.44 (14.82)	37.35 (14.82)	$p < .0001$

Rescue Medication Use & Treatment Satisfaction

Subjects in the NSAID arm used an average of 13.39 (10.80) dosages of rescue pain medication over the 4 weeks compared to only 6.73 (9.03) dosages for the PSWT arm or a difference of 6.73 (1.41) in favor of the PSWT ($p < 0.0001$). The distribution of rescue pain medication use was markedly different with 44% of the PSWT arm using no rescue medication compared to 13% of the NSAID arm. This difference is statistically significant ($p < 0.0001$). Subject satisfaction was found to be greater in the PSWT with an average rating of 76.39 (19.84) compared to an average rating of 59.55 (21.86) in the NSAID arm, a difference that is statistically significant ($p = 0.0001$)

Adverse Events

Adverse events (AEs) associated with NSAID or PSWT use were assessed during the study period and recorded at the end of the study (Table 4). In the NSAID arm, 2 subjects reported serious AEs of peripheral edema and hypertension, following which Etoricoxib treatment was ceased. There were 9 minor AEs in the NSAID arm, however these subjects chose to continue NSAID therapy after consulting with the PI. There were no AEs reported in the PSWT arm – the sole dropout in this arm did so at the beginning of the study, citing a preference for pharmacotherapy.

Table 4

Distribution and description of the Adverse Events in the two treatment arms.

Treatment Arm	Adverse Events/ Subjects	Event
PSWT	0/0	0
NSAID	11/9	• peripheral edema (n = 1) • gastric upset (n = 3) • hypertension (n = 5) • dysuria (n = 1) • increase in serum creatinine levels (1.5 mg/DL to 3.5 mg/DL) (n = 1)

Dose-Response Characteristics (Post-hoc Analyses)

The three ANCOVA analyses reported above found treatment effectiveness (final 4-week score) was observed to be inversely proportional to subject BMI in all three cases. However, these analyses assumed the same loss of effectiveness for both treatment types as a function of BMI. The mechanism of action differs across the two arms. PSWT is a method of high-frequency magnetic stimulation, which utilizes a dipole magnetic field antenna. The decay of the magnetic field of the PSWT antenna (along the z-axis perpendicular to the antenna), B_z can be characterized as:

$$Equation1 \qquad B_Z = \frac{KR^2}{(Z^2+R^2)^{3/2}},$$

where R = radius of the antenna, Z = distance of the target away from the plane of the antenna and K is a constant. The subject PSWT device used in the present study has a radius of 6 cm.

The neck circumference is a useful predictor of BMI [38]. Moreover, the neck circumference can be used to calculate the diameter of the cross-section of the neck and thus estimate the depth of the PSWT target region (cervical spine) for various BMIs. For instance, a normal neck size (i.e. for a 20 BMI person) is about 38.1 cm, while a 30 BMI person's neck size is about 43.2 cm. This implies that the cervical spine is located at a depth of 5.6 cm and 6.3 cm respectively from the skin for these two individuals. Inserting these values into Eq. 1 indicates that the field intensity at the cervical spine of an individual with a BMI of 20 would be about 21% greater than the field intensity for a person with a BMI of 30. As such, this leads us to postulate that the treatment effectiveness (analogous to dose responsiveness) of PSWT should be about 21% greater a 20 BMI person compared to a 30 BMI person.

To test this premise we conducted three separate univariate regression analyses for both the NSAID and PSWT arms, one for each of the outcome measures. The dependent variable (DV) in each regression is the reduction in relevant outcome measure (in this case baseline minus 4-week), and the independent variable is the subject's BMI. In all six of these analyses we find the outcome measures were negatively correlated with BMI (Table 5). Using these coefficient estimates, it is possible to estimate the change in outcome measure score for various BMIs for each of the outcome measures. For instance, we calculate that a 20 BMI person using NSAID's can expect to see a 43.69 points reduction in VAS_{active} (52.75 − .453*20) = 43.69). However, if the person had a BMI of 30 the reduction would only be 39.16 points (52.75-.453*30). This implies the effectiveness (dose response ratio) of the NSAID is 12% (= 43.69/39.16) more effective when comparing a 20 BMI person to a 30 BMI person. Similarly, the figures for a person using PSWT would be a reduction of 57.85 VAS points if the person's BMI was 20 and 50.98 if the person's BMI was 30. This implies the device's dose response ratio is 1.134 = 57.85/50.98 or 13.4% more effective for the 20 BMI person compared to the 30 BMI person (Table 5). The dose response ratio estimates for the NSAIDS vary from 1.07 to 1.21, mainly because the regression coefficient for BMI was not always significant. In contrast the estimate for dose response ratio for PSWT was very stable, ranging from 1.13 to 1.15 in line with our theoretical estimate of 23% derived earlier.

Table 5
Coefficients for the univariate regression of BMI for the various outcome measures.

Treatment Arm	Regression Coefficients	
	Intercept	BMI
	Neck Disability Index (NDI) (0–50 points)	
NSAIDS	19.21	− .247
PSWT	18.99	–.105
	Visual Analog Scale (VAS)- Rest (0-100 mm)	
NSAIDS	47.06	− .296
PSWT	70.10	-732
	Visual Analog Scale (VAS)- Activity (0-100 mm)	
NSAIDS	52.75	− .453
PSWT	71.58	-687

Also investigated was the relationship between rescue medication use and the reduction in pain. We did this using regression analysis, with the DV being rescue medication use and the independent variables being standard demographics, baseline VAS_{active} pain level and the change in VAS_{active} pain level. The only statistically significant demographic variable was age, with older subjects using more rescue medication. However, both baseline pain and pain reduction were also significant, indicating that those with higher baseline pain used more medication and importantly those experiencing the largest pain reduction used less medication.

Discussion

NSAIDS are a first-line treatment for managing pain and inflammation resulting from osteoarthritis, including COA. However, the adverse effects associated with long term use of this treatment regime, such as GI and cardiovascular complications, have led to a search for alternative therapies. As a result, there is growing interest in the medical community to deploy non-pharmacological interventions such as medical devices for managing chronic pain[25]

This is the first study we are aware of that investigated PSWT as a primary treatment for a chronic disease state against another first-line treatment. Prior clinical studies have investigated the effectiveness of PSWT as part of multimodal therapies, both in randomized, placebo-controlled trials (RCT) and large registry studies [31, 33, 34, 39]. Notably, in a four week RCT on knee osteoarthritis where patients continued the use of prescribed NSAIDS (as needed), 26% discontinued NSAID use in the PSWT arm compared to 3% in the placebo control arm[29]. Chronic pain patients (varying etiologies) who used PSWT as an adjunct therapy reported in three different registry studies a decreased reliance on pharmacotherapy within 7 days of using the intervention[31, 33, 34], and also in a prospective study of six months duration (37).

Participants in this study on average were in pain for about 2 years, indicated that they were in severe pain, and were at the border between being classified as being moderately and severely disabled. This was confirmed by radiological imaging where all but 7% of the samples scored OA grade 2 or higher. In addition, they were recruited after seeking specialist medical assistance. Thus, this sample of subjects can be viewed as chronic pain sufferers who were at least moderately disabled, were in severe pain, and who had yet to find a treatment to alleviate this pain. Following 4 weeks of treatment, subjects in both treatment arms reported statistically ($p < 0.0001$) and clinically significant reduction in

disability (NDI) and pain level (VAS_{rest} and $VAS_{activity}$), where clinical importance was defined as a 7.5 point reduction (0–50 points) for NDI [40] and 20 mm reduction (100 mm scale) for VAS [41]. Specifically, the average patient no longer was classified as being even moderately disabled and the pain level for the PSWT arm was in the mild range and in the low moderate range for the NSAID arm. Importantly the PSWT arm reported statistically significant greater reductions for all three of these measures compared to the NSAID arm. This group, in addition to not taking any prescription NSAIDs during the 4 week study, also reported using approximately 50% less rescue medication compared to the NSAID arm ($p < .0001$). In fact, 44% of the PSWT arm didn't use any rescue medication compared to 14% for the NSAID arm. Finally, the PSWT group reported significantly greater overall satisfaction.

Providing non-pharmacological alternatives to NSAIDs in managing COA could also have economic advantages. One recent study indicated that up to 31% of costs in managing arthritis patients can be attributed to NSAID-related complications [42]. Another study indicated that more than 100,000 patients are hospitalized due to NSAID-related GI adverse effects each year, with direct costs between $1800 and $8500 per patient per hospitalization. In the elderly alone, NSAID-related GI adverse effects were reported to cost more than $4 billion a year in the US [43]. Similarly, in the UK the cost to each Patient Care Group (now known as Clinical Commissioning Groups (CCGs)) due to NSAID-related GI adverse effects averages £433,000, or an estimated total of £251 million to the UKs National Health Service [44]. In this study 9subjects (9%) in the NSAID arm reported adverse events, with 2 subjects withdrawing from the study due to adverse events. No adverse effects were reported in the PSWT arm. Moreover, no serious adverse side effects associated with the use of PSWT have been reported across a variety of chronic pain etiologies and for study periods up to six months [28–31, 33, 34, 39]. Minor adverse effects that have been reported were related to method of attachment to the skin (taping, application by wraps etc.). While the data used to gauge the possible magnitude of adverse effects associated with PSWT therapy is relatively small (hundreds of patients from clinical trials and tens of thousands from registry studies), the method of application and mechanism of action associated with PSWT indicates that the risk of adverse side effects is low. This is a major advantage when compared to pharmacological treatments such as NSAID which have been shown to dramatically increase the cost of treatment of chronic disease such as arthritis, due to the significant number of adverse side effects.

The believed mechanism of action of PSWT therapy is magnetic neuromodulation [45], although the precise pain signaling pathways involved are still being elucidated. However, the observed influence of BMI on efficacy may serve to help identify the specific responding tissues to the stimulation. Specifically, using the decrease in efficacy of the device it is possible to calculate the depth below the skin where the PSWT is working. This depth appears to be the nerves running up the spinal cord.

Limitations

A lack of a placebo control is a limitation in this study, but it is now being acknowledge that the placebo effect is built-in to any given treatment[46]. Prior chronic pain placebo controlled trials using this device reported modest placebo effects[29, 30] and the device performs better than placebo in acute pain studies [27, 28, 47] suggesting that the efficacy of the device is not only driven solely by the placebo effect. Furthermore in this study we find the reduction in efficacy of both treatments being associated with the subject's BMI, especially for the PSWT arm, to be strong evidence of device efficacy since this association should be independent of the placebo effect, and instead be due to the proposed mechanisms of action associated with both treatments. However further study is needed to confirm the magnitude of the placebo effect in COA as well as determine the durability of treatment. The study duration was relatively short, lasting only 4 weeks of treatment. While a recent study demonstrated the durability of PSWT treatment effectiveness over a 6-month period[39], subjects in that study utilized PSWT treatment as part of multi-modal therapy. As such longer term studies are warranted.

Conclusion

Both NSAID therapy and neuromodulation therapy using PSWT resulted in statistically and clinically important reductions in pain level and improvement in functionality associated with cervical osteoarthritis, when used for 4 weeks. However, the PSWT intervention demonstrated superior improvements in all outcome measures when compared to the Etoricoxib therapy arm, including patient satisfaction rating and decreased use of rescue pain medication. These results suggest that neuromodulation using PSWT may be a superior pain treatment option, when compared to COX-2 NSAIDS for neck osteoarthritis, and as well, represents a non-invasive, non-pharmacologic treatment option.

List Of Abbreviations

COA: Cervical Osteoarthritis

KOA: Knee Osteoarhtritis

NDI: Neck Disability Index

PSWT: Pulsed Shortwave Therapy

VAS: Visual Analog Scale

Declarations

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Contributions

RM and OT implemented the study and oversaw data collection. IR and OT contributed to the design of the study. RS and SK contributed to the statistical analysis of the data. IR, RS, KM and SK provided data interpretation as well contributing to the drafting and editing of the paper for intellectual content. IR takes responsibility for the integrity of the study from beginning to finalization of the completed article.

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Ethics declarations

The study was approved by the ethics review board of New Mazloum Hospital, Tripoli, Lebanonand written informed consent was obtained from all participants involved in the study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the correspondingauthor on reasonable request.

Competing interests

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Clinicaltrials.gov (NCT03542955)

Date of Registration May 18th 2018

https://clinicaltrials.gov/ct2/show/NCT03542955?cond=neck&cntry=LB&draw=2&rank=5

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Figures

Figure 1

Application of ActiPatch® to the cervical region of the neck. There is no paresthesia or warming sensation while the device is being used.

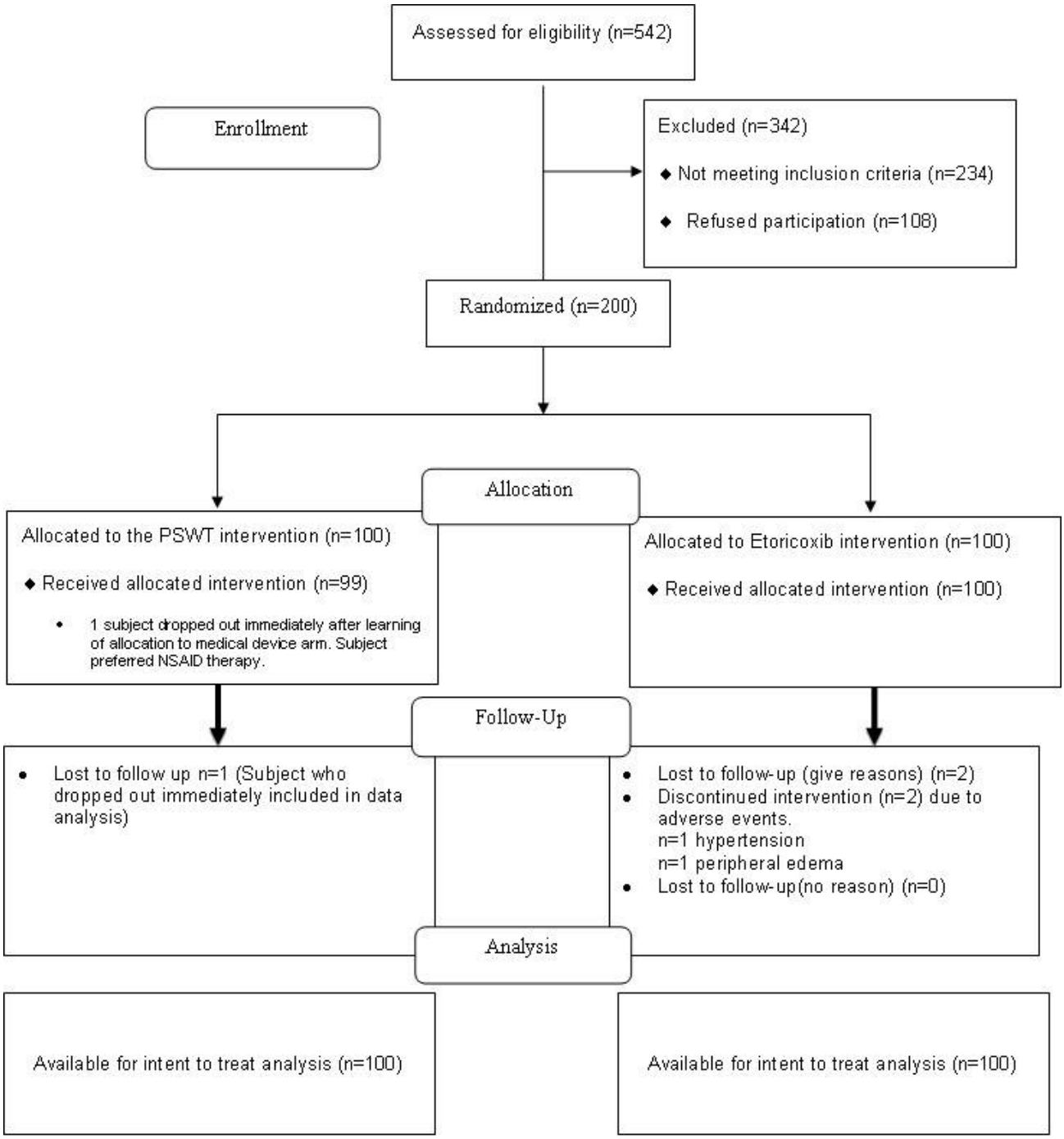

Figure 2

Subject Flow Diagram

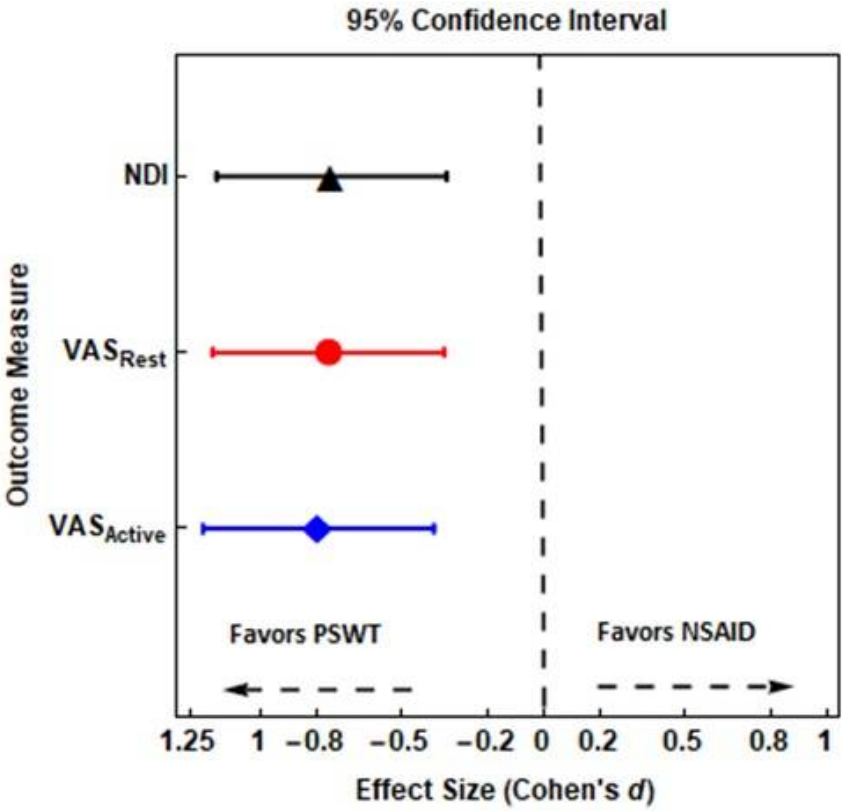

Figure 3

Standarized effects size for the three outcome measures: NDI -0.74 (95% CI-1.16 to -0.34), VASrest -0.77 (95% CI -1.17 to-0.35) and VASactive -0.796(95% CI -1.20 to -0.39).

Supplementary Files

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