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Protocol

The hypoalgesic effects of wrist extensors training with blood flow restriction in patients with lateral elbow tendinopathy: a study protocol for a cross-over randomized controlled trial

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ABSTRACT

Background: Lateral elbow tendinopathy (LET) is a disabling overuse injury with a significant healthcare burden. Despite the fact that exercise interventions are considered the best recommended treatment option of LET, their effectiveness in reducing pain and improving function remains debatable. The aim of our study is to evaluate the immediate effects of a new method of exercise using blood flow restriction (BFR) on pain perception and pain-free grip strength in patients with LET.
Methods: This study was designed as a cross-over randomized controlled trial. We will compare an intervention using wrist extensors training with (WET-BFR) to a control intervention using WET-without-BFR in patients with LET. All measurements will be taken by a blinded assessor pre- and post-intervention. Primary outcome measures will be the changes in pressure pain thresholds at the lateral epicondyle, extensor carpi radialis brevis, C4 vertebra and tibialis anterior. Secondary outcome measure will be the changes in pain-free grip strength ratio.
Conclusions: New approaches are needed to improve the treatment outcomes in LET. Although BFR training was found more effective in improving function and treatment success than conventional training, the effects on pain intensity were poor. Our hypothesis is that using the best BFR practice guidelines for wrist extensors training might be more effective to reduce pain sensitivity compared with non-BFR training in patients with LET. The trial will provide new research data to inform clinical practice regarding the effects of using BFR training in the current patient group.
Trial registration: University of West Attica ethics committee: 9150/01-02-2023, ClinicalTrials.gov: NCT05919914

Keywords: Exercise, Hypoalgesia, Pressure pain threshold, Tennis elbow

INTRODUCTION

Lateral elbow tendinopathy (LET), commonly referred to as tennis elbow, is the most common musculoskeletal problem of the elbow.[1] It affects approximately 1-3% of the general population predominantly between the ages of 45 and 54 years.[1,2] LET mainly describes pain over the lateral epicondyle due to tendinopathic changes on the common wrist extensors origin.[2,3] It is often caused by an overuse injury or direct trauma in the lateral epicondyle.[4] Patients with LET present with increased pain during griping, significant functional decline and substantial productivity loss.[5] Despite the ongoing research evidence in the treatment of LET, the best-effective management of the condition remains inconclusive possibly due to the complex underlying pathophysiological mechanisms.[6,7]

For the appropriate management of LET, a range of non-surgical options is recommended, including activity modification, braces, exercises, physiotherapy modalities, acupuncture and corticosteroid injections.[6-8] An exercise programme is considered the key intervention to reduce pain and improve function.[9] However, evidence suggests that exercise interventions provide a small clinical benefit compared with passive interventions or control in all outcomes at the long-term follow-up.[8,9]

Based on a recent randomized controlled trial, a new type of exercise using BFR had clinically better results in function and self-perceived recovery compared to non-BFR training in patients with LET.[10] Despite the positive outcomes, the effects of BFR in reducing pain intensity were poor.[10] Possibly, this was attributed to the BFR training protocol (3 sets of 10 repetitions) for the wrist extensors which differed from the best BFR practice guidelines (30-15-15-15 repetitions).[10,11]

Several studies have advocated that BFR training produces significant reductions in pain sensitivity in healthy individuals and patients with anterior knee pain.[12-15] Notably, these hypoalgesic responses have been explained by local and central mechanisms such as the endogenous opioid and endocannabinoid system pain modulation mechanisms.[14,15] According to one case report, a single intervention of WET-BFR using 30-15-15-15 repetitions presented a substantial decrease in pressure pain thresholds (PPTs) at the lateral epicondyle (>21%) immediately after treatment. However, the current study results should be interpreted with caution due to the nature of the study methodology. It seems that further research using a comprehensive methodology is required to evaluate the possible hypoalgesic effects, if any, of WET-BFR in patients with LET.

The main objective of our study is to evaluate the effect of wrist extensors training with BFR (WET-BFR) compared with the same program without BFR on pain perception in patients with LET immediately post-intervention. Also, the changes in pain-free grip strength between the interventions will be evaluated as a secondary outcome measure. The research question for this randomized controlled trial will be: Would WET-BFR be more effective in reducing PPTs compared with WET-without-BFR in patients with LET immediately after intervention?

METHODS

Study design

We aim to conduct a randomized controlled trial with a cross-over design.

Study population and setting

The population of the study will be adults up to 60 years old. Data collection will be performed at multiple physiotherapeutic clinics in Athens, Greece from February 2023 to June 2024. The study has been approved by the research ethics committee of the university of West Attica (9150/01-02-2023) and registered prospectively in the ClinicalTrials.gov (NCT02664714).

Participant recruitment

Participants will be recruited via electronic invitations at the university of West Attica and physiotherapeutic clinics based in Athens, Greece. Participants will receive appropriate information about the research and will freely sign a consent form before their participation. At the initial visit, they will be assessed for eligibility by a musculoskeletal physiotherapist (SK) with 18 years of experience. The diagnosis of LET will be based on the following tests: pain on palpation over the lateral epicondyle, positive Cozen's, Maudsley's, and/or Mill's test.[16]

Eligibility criteria

Patients diagnosed with LET, both men and women, with symptoms lasting over two weeks will be included in the study. Patients with shoulder tendinopathy; cervical radiculopathy; rheumatoid arthritis; neurological deficits; radial nerve entrapment; a history of cardiovascular disease, cancer or breast surgery; orthopαedic surgeries during the past six months; thrombosis or venous deficiency; body mass index ≥ 30; Crohn's syndrome, or a family or personal history of pulmonary embolism will be excluded from the study.

Randomization and masking

The participants will be randomly assigned to one of two sequences at a 1:1 ratio: i.e., in the experimental condition (WET-BFR) followed by the control condition (WET-without-BFR) or the control condition followed by the experimental condition. A computer-generated randomization software (https://www.randomizer.org/) will be used for the random assignment of the interventions. The process will be carried out by a researcher not involved in the data collection, aiming to keep group allocation concealed from the patients, therapist, assessor and data analyst. An administrative assistant will be responsible for contacting and group allocation of the patients to each condition using sealed, opaque envelopes. A flow chart showing the allocation of the participants and follow-ups is depicted in Figure 1.

Due to the trial design (cross-over) and the nature of the interventions, the physiotherapist and patients will not be blinded to group allocation. However, a blinded assessor (IL) will record the demographic characteristics, such as age, duration of symptoms, body mass index, previous symptoms, dominant/painful side, the disability score using the patient-rated tennis elbow evaluation questionnaire (PRTEE), blood pressure, PPTs, and pain-free grip strength at baseline. The Greek version of the PRTEE questionnaire is a condition-specific patient-reported outcome measure that captures pain and disability in LET.[17,18] Its score can range from 0 (no pain and disability) to 100 (worst pain and disability).[19]

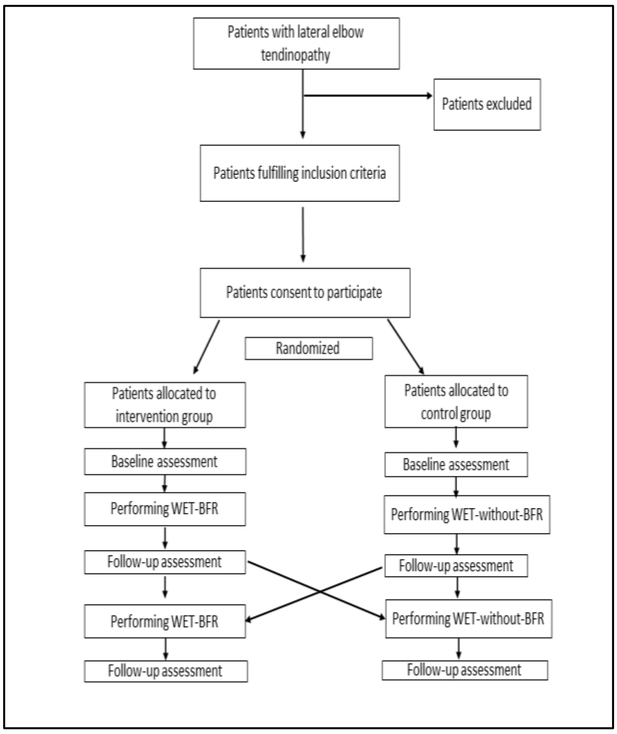

Figure 1: Study flow diagram for allocations and follow-up.

The same assessor will evaluate outcome measures after wrist extensor exercises (blood pressure, PPTs and pain-free grip strength). To ensure the blinding of the assessor, the assessment room will be located away from the place providing the interventions and the participants will be prompted to keep the type of interventions concealed.

Interventions

Participants will perform an exercise of the wrist extensors using BFR at 40-50% of complete arterial occlusion pressure or the same exercise without BFR in a randomized order. Interventions will be separated by one week. To determine the load of the wrist extensor exercise, at the start of each session, the participants will perform 5-10 warm-up repetitions with a free weight using a pain-monitoring approach (acceptable pain during the exercise<2 out of 10 in a numeric pain rating scale).

For the BFR application, an automatic tourniquet system (Mad-Up Pro, France) will be used. For the WET-BFR intervention, the arterial occlusion pressure will be determined in the standing position (calibrated).[20] Before calibration, the participants will rest in the standing position for three minutes to ensure restoration of blood flow circulation. Then, an appropriate cuff will be placed in the most proximal part of the upper limb (Figure 2). The WET-BFR session will include four sets (30-15-15-15 repetitions) of wrist extensions (concentric-eccentric) with the elbow extended (Figure 2). The pace of exercises will be kept using a metronome (two seconds for each contraction). We will use a 30-second break between the sets, keeping the cuff inflated during resting periods. Any adverse events will be recorded via personal or telephone communication following the intervention.

Figure 2: Wrist extensors training with BFR (30-15-15-15 repetitions).

For the control condition, the participants will execute the same exercise of the wrist extensors without BFR. The conditions regarding position, load, pace, sets, repetitions and break periods will be the same as the experimental intervention. At the end of each exercise program, wrist extensor stretching will be performed (3 times×30 seconds).

Outcome measures

The primary outcome measure will be changes in PPTs before and after interventions. PPTs will be measured in a seated position using a hand-held digital algometer (Baoshishan ZP-1000 N 20/22806, China). Measurements will be collected in the same order on each occasion, starting from the non-dominant side to the dominant side, at the following sites: the lateral epicondyle, the extensor carpi radialis brevis (4 cm from the lateral epicondyle), the transverse process of the C4 vertebra, and the tibialis anterior. The mean value (kg/cm^2) of three measurements at each site will be calculated. A 20 to 30-second rest period will be used between the administrations. Before measurements are taken, a familiarization process of testing PPTs will be conducted in 10 healthy subjects to calculate intra-rater reliability.

We will include the pain-free grip strength test as a secondary outcome measure. The test has presented excellent reliability in patients with LET (Intraclass correlation coefficients=0.86-0.96).[21] We will use a Jamar hand dynamometer, calculating the mean value (kg) of three contractions with a 30-second break between the efforts. Patients will perform the test before and after each intervention lying supine with the elbow fully extended.[18,22] The minimal clinically important difference of the test in patients with LET is seven kgs.[8] The measurements will be presented as a ratio between the result of the affected elbow and the maximum grip strength of the unaffected elbow.[23]

We will evaluate the systolic and diastolic blood pressure before and after each intervention. Measurements will be conducted in a seated position at the brachial artery using the Omron M6 Comfort HEM-7321. We will conduct two measurements with a 30-second rest period and the average value will be calculated.[20,24]

We will use the Borg 6-20 scale to measure perceived exertion. Borg 6-20 scale is simple self-administered tool designed to measure effort and exertion during exercise with excellent reliability and validity.[12,25] The participants will be asked to rate their effort after each set of exercises from 6 (no exertion) to 20 (maximal exertion).[25]

Sample size

For the sample size calculation, we have used the GPower 3.1. PPTs were the primary outcome measures with an expected effect size of 1.00.[26,27] Setting the power of the study at 0.80 and a two-sided significance level at 0.05, a sample size of 17 patients was estimated to be sufficient for our study aims.[10] Nonetheless, a sample size of 20 per group was considered appropriate to allow for a 10% loss to follow-up.

Statistical analysis

Data will be analyzed using the IBM statistical package for social sciences version 25. We are going to check the normality of the data using Q-Q plots and the Shapiro-Wilk test. Participants' baseline characteristics will be summarized using means, standard deviations and ratios. Between-group differences will be analyzed using mixed-effects models. We will use participant-specific random effects over the pre- and post-intervention measurements. The fixed effects will include group, time, and group × time interactions. The parameter estimates will be adjusted for covariates such as sex, age, body mass index, changes in blood pressure, duration of symptoms and baseline functional disability (PRTEE score). The rating of perceived exertion will be assessed using a repeated-measures ANOVA test. Also, we will calculate Cohen's d-effect sizes by using the pooled standard deviations of the baseline scores.

DISCUSSION

Our report presents rationale and design of a randomized controlled trial investigating immediate effects of WET with and without BFR on pain perception in patients with LET. Results from this study may directly inform clinical practice by providing evidence about the efficacy of BFR training in reducing pain sensitivity and improving function in LET immediately after intervention.

Research evidence advocates significant improvements in muscle strength, hypertrophy and function in favor of BFR training compared with non-BFR training in a range of musculoskeletal pathologies such as anterior knee pain, knee osteoarthritis, tennis elbow and patients after anterior cruciate ligament (ACL) reconstruction.[28-32] However, the effect of this novel type of exercise on pain intensity remains unclear. For example, although the addition of BFR to resistance training provides better outcomes than conventional training in the recovery after ACL reconstruction, there are no clinical improvements in favor of BFR in the management of knee osteoarthritis.[31,33,34] This contradiction has been attributed to several factors such as the pathophysiology of the condition, severity of symptoms or BFR methodology.[11]

Previous trials have suggested that the BFR component may produce a within-session pain modulation mechanism that can benefit patients by allowing them to perform more intensive training with less pain during rehabilitation.[10,31] The pain modulation mechanisms involved may include several pathways such as central descending pain inhibition from the cortex and thalamus, conditioned pain modulation, motor control unit activation, stimulation of baroreceptors, the production of secondary metabolites, and psychological input.[11,14]

CONCLUSION

Although low-intensity BFR training was found effective in increasing the pain threshold in healthy individuals, similar trials in populations with pain symptomatology are lacking. To our knowledge, our study will be the first to adopt the best available BFR clinical recommendations to evaluate the effectiveness of the method in PPTs in a population with pain symptomatology such as LET.

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