ABSTRACT

Introduction Although compression is used to control pain in knee osteoarthritis (KOA), its clinical application is poorly supported, and there is a lack of scientific evidence to support its clinical use. As a low-cost and accessible protocol, compression using elastic bands could be a non-pharmacological intervention to reduce pain and improve physical function in individuals with KOA. This study aims to evaluate the effects of compression on pain and function in individuals with KOA.

Methods and analysis A randomised controlled clinical trial will be conducted. Individuals with KOA (n=90; both sexes; between 40 and 75 years old) will be allocated to three groups (n=30/group): compression (compression by the elastic bandage on the affected knee, once a day for 20 min, on four consecutive days); sham (same protocol, but the elastic band is placed around the affected knee without compression) and control (no intervention). The individuals in the three groups will be evaluated 1 day before the first intervention, 1 day after the last intervention, and at the 12th and 24th weeks after the end of the intervention. Pain intensity by the Visual Analogue Scale and pain scale from Western Ontario & McMaster Universities Osteoarthritis Index (WOMAC) will be the primary outcomes. The secondary variables will be physical function assessed by the WOMAC questionnaire and physical tests (step test; 30 s sit and stand test; 40 m accelerated walk test). The Global Rating of Change Scale (GRC) will also be applied to quantify the volunteers’ perceived change.

Ethics and dissemination The project was approved by the Human Research Ethics Committee of the Federal University of São Carlos, São Paulo, Brazil (3955692). The results will be published in peer-reviewed journals.

Trial registration number NCT04724902.

INTRODUCTION

Knee osteoarthritis (KOA), representing an average cost of US$15 000 /year per user, is radiographically present in 30% of individuals over 45 years old and symptomatic in at least half of these cases. It is characterised as chronic and progressive and is one of the main causes of musculoskeletal pain and functional disability. Among the treatment options, a combination of pharmacological (paracetamol, non-steroidal anti-inflammatory drugs and topical agents) and non-pharmacological interventions (patient education; weight reduction, when necessary; physical exercise and physical therapy) is recommended.

Even though physical exercises constitute the basic treatment of KOA, pain management is important for initiating and adhering to treatment. Among the non-drug alternatives, the use of a knee brace is common in this population. Although compression is used to control pain in KOA, for example, the use of knee braces and associated with the application of physical agents, a review showed that its effect is moderate and low for pain relief and improvement of function, respectively, in individuals with KOA. Thus, despite compression being...
recommended and widely used, its clinical application is poorly supported because of the scarcity and heterogeneity of protocols, and there is still a lack of scientific evidence to support its clinical use.

The floodgate theory can explain the possible mechanism of action of compression in pain relief, according to which pain can be modulated by the stimulation of tactile receptors in the skin. In addition, aspects such as improved proprioception may be present and promote beneficial functional effects, such as better stability during movement. In this context, compression may be a low-cost and easy-to-apply alternative for pain control and functional improvement in people with KOA.

This study presents the design of a randomised study whose objective is to analyse the effect of compression on the pain and function of individuals with KOA. Our hypothesis is that compression will effectively reduce pain and improve function in these individuals.

**MATERIALS AND METHODS**

**Patients and public involvement**

The patients and the general public were not involved in the planning, designing, conducting, reporting or dissemination of this study.

**Study design and setting**

The study consists of a non-probabilistic, convenient and intentional single centre randomised controlled clinical trial. This study was designed and will be conducted according to the guidelines recommended by Template for Intervention Description and Replication, the OARSI recommendations for clinical trials with KOA patients and in accordance with the recommendations outlined in the Standard Protocol Items: Recommendations for Interventional Trials. Randomised trials will be reported following the guidelines of the Consolidated Standards of Reporting Trials for non-pharmacological studies. Four evaluations will be performed: two immediately before and after the application of the therapy and two follow-up evaluations at 12 and 24 weeks. The evaluation and intervention periods are shown in figure 1. A ‘blind’ evaluator will carry out all evaluations without information about the identification of the group to which the volunteer belongs. The procedures will always be carried out simultaneously for each volunteer during the intervention and evaluation days so that the same time interval between interventions and evaluations is respected. All participants will be instructed not to start any other treatment during the study period. In addition, they will receive a diary describing the drugs that will be used (name, dosage, frequency and route of administration) during the study period.

**Participants**

Volunteers will be recruited from public announcements and waiting lists from local and regional physiotherapy, rehabilitation, orthopaedics and rheumatology outpatient clinics, as well as from an existing list of volunteers diagnosed with KOA available in our laboratory. In this project, 90 volunteers of both sexes, aged between 40 and 75 years, diagnosed with KOA according to the clinical and radiographic criteria of the American College of Rheumatology will participate. The subjects will undergo a radiographic examination of both knees, with profile, anteroposterior and axial views. Volunteer screening will be carried out by a physical therapist specialising in the subject and with experience in evaluating individuals with KOA.

Individuals who will be included in the study are required to present with signs of OA in at least one of the compartments of the knee joint (tibiofemoral and/or patellofemoral joint), grade 2 or 3, according to the Kellgren & Lawrence criteria in the radiographic examination of KOA and a minimum score of 4 cm on the Visual Analogue Scale (VAS, total of 10 cm). In the case of bilateral KOA, only the knee with the highest level of symptoms will be randomised as long as it meets the inclusion criteria. In addition, individuals who present with at least one of the following criteria will be excluded: regular practice of moderate or intense physical activity for more than 45 min per week; have started physical activity or performing any physical therapy treatment in the previous 3 months; use of corticosteroid injection in the knee (6 months prior); previous knee or hip surgeries and/or any clinical restriction that makes it impossible for them to participate in the proposed evaluations or interventions: compression (elastic bandage with compression) and sham (elastic bandage without compression) groups.

**Figure 1** Study design. Assessments: pain intensity (VAS); physical functionality questionnaire (WOMAC); change perception scale global (GRC) and tests in occupation physics (test of step, test in to sit and rise gives chair in 30 s, 40 brisk walk test metres). Interventions: compression (elastic bandage with compression) and sham (elastic bandage without compression) groups. VAS, Visual Analogue Scale; WOMAC, Western Ontario & McMaster Universities Osteoarthritis Index.
intervention (cardiorespiratory, neurological, musculoskeletal, vascular changes and/or the presence of skin lesions from the application of the bandage).

Interventions

The compression intervention protocol is based on a previously accepted methodology that was developed in our laboratory. To standardise the level of compression presented, a previous reliability study was performed (n=10) with the aid of a pressure gauge (Stabiliser - Chattanooga Group) positioned on the knee between the patient’s skin and the elastic bandage. The manometer was inflated to a value of 40 mm Hg, the value indicated by the manufacturer as the pressure at rest of the pneumatic bag, and the knee was then wrapped with the bandage. The number of turns of the tensioned elastic bandage required to wrap the knee to reach the indicated compression range (30 mmHg ≤ x ≤ 60 mm Hg) was noted, and, if necessary, more than one band could be used. The level of compression that the sham group would receive with the untensioned bandage was also evaluated. In both groups, the circumference of the knees was measured at three points (popliteal fossa, 10 cm above and 10 cm below) and the number of turns with the bandage.

This first step was performed in a test-retest format, with an interval of 7 days, so that it was possible to calculate the level of intraevaluator reliability, which indicated a Kappa coefficient of 0.625, considered a substantive agreement. From the reliability study, it was possible to calculate the average number of turns to be performed in both the compression and sham groups so that the compression level was maintained within the stipulated range. In the compression group, all patients used a bandage, with a mean of 5.7 wraps (range, 5–7 wraps) and a maintained pressure level of 48 mm Hg (range, 46–52 mm Hg). In the sham group, all of them also used a bandage with an average of 4 wraps (range, 3–5 wraps), and the pressure level was maintained at 0 mm Hg.

Compression protocol

To apply compression, the volunteer must remain in the supine position on a stretcher with both lower limbs extended and relaxed. The intervention in the compression group will be performed with elastic bandages (Selecta 13 cm × 160 cm, composed of 45% cotton, 20% elastodiene and 27% polyamide) covering the entire surface of the knee, positioned considering anatomical aspects: covering the femoral condyles and anterior tuberosity of the tibia (figure 2). The bandage will wrap the knee from distal (tibial tuberosity) to proximal (femoral condyles), respecting the blood flow of venous return and without restricting blood flow. The level of compression was defined following recommendations in the literature on interventions for compression in lymphedema and venous disorders and should be maintained between 30 and 60 mm Hg. Variations within the stipulated minimum and maximum values may be changed according to the volunteers’ self-report, indicating a moderate, comfortable and pain-free level of compression. The occurrence of any sign of venous stasis (redness and/or oedema) may also indicate the need for a reduction in the level of compression or interruption of the procedure. The intervention will be performed for 20 min, once a day, for four consecutive days (figure 1).

Sham protocol

The sham group will receive the same procedure performed in the compression group; however, the bandage will not be tensioned, that is, it will only gently wrap the knee joint with KOA.

Control protocol

The control group will be composed of individuals with KOA who will not receive any type of intervention and will undergo the evaluations at the same time intervals as the other groups. In addition, they will be instructed not to start another treatment during their participation in the project.

Outcome measurements

Assessments will be performed by a physical therapist who will be blinded to the allocation of each volunteer. Pain is the primary variable of the study and will be assessed using the VAS and Western Ontario & McMaster Universities Osteoarthritis Index (WOMAC) pain domain. As secondary variables, the domains of rigidity and physical
dysfunction of the WOMAC—physical stiffness and dysfunction scales, as well as functional physical tests: sit and stand test, 30 s17 52; step test; 40 m (4×10 m)) accelerated walk test.52 The Global Rating of Change Scale will also be applied to quantify the volunteers’ perceived change in overall status.53 A detailed description of the instruments for evaluating the variables, as well as the evaluation moments, is presented in table 1.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Description of assessment instruments</th>
</tr>
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<tbody>
<tr>
<td><strong>Variables</strong></td>
<td><strong>Instructions</strong></td>
</tr>
<tr>
<td>Visual Analogue Scale</td>
<td>The scale will be visually available to the individual so that he can classify the average pain intensity for the last week, and before and after each functional physical test.</td>
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<tr>
<td>Western Ontario &amp; McMaster Universities Osteoarthritis questionnaire</td>
<td>Self-report questionnaire designed to assess problems experienced by individuals with lower limb OA in the last 72 hours. The questionnaire contains 24 questions, which comprise three domains: pain, stiffness and physical function.50 61</td>
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<tr>
<td>Chair sit-up test 30 s</td>
<td>The test will be performed using an armless chair, with a seat height of approximately 43 cm from the floor. The participant will sit in the chair, with a straight back, feet apart, shoulder-width apart and resting on the floor at an angle slightly behind the line of the knees. The arms should remain crossed against the chest and to help with balance, one foot may remain slightly in front of the other.49</td>
</tr>
<tr>
<td>Step test</td>
<td>The individual will be positioned in front of the stairs, and by voice command will be guided to go up the nine steps and go down again. Each step will be 20 cm high, and it will be allowed to use the handrail as a safety instrument.</td>
</tr>
<tr>
<td>40 m accelerated walk test (4×10 m)</td>
<td>Participants will be asked to walk as quickly, safely, without running, 10 m from one cone, then turn around in a second cone, return and repeat the process until the 40 m mark.63</td>
</tr>
<tr>
<td>Global Rating of Change</td>
<td>It’s use has been recommended for the outcome of chronic pain, mainly in clinical trials aiming at better applicability of the results in clinical practice. It is used to quantify the patient’s improvement or worsening over time, according to the patient’s perception. The volunteer will be asked to assess their current health status, associated with knee pain, compared with the preintervention period.53</td>
</tr>
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</table>

**Randomisation**

Individuals included in the study will be stratified by sex and randomly divided using a digital tool (www.randomization.com). Three groups will be randomised with 30 individuals each: compression, sham and control. Concealment will be adopted to avoid selection bias using an opaque, non-translucent and sealed envelope.26 Furthermore, the group to which an individual belongs
will only be revealed immediately before the intervention. After the completion of the evaluations, individuals from the three groups will be referred to face-to-face training (if available) and will receive a booklet consisting of therapeutic exercises recommended for the treatment of KOA.

Sample size
The sample size was preliminarily calculated using the G*Power software (V.3.1.3; University of Trier, Germany). Two calculations were performed: pain (assessed using the VAS) and function (assessed using the WOMAC questionnaire). The calculation was based on the application of an F-test for the difference between the three independent means (three groups). The effect size considered for this calculation, based on a previous study, were $d=0.45$ for EVA and $d=0.39$ for WOMAC, which after conversion represented $f=0.225$ and $f=0.195$, respectively. The effect sizes were between small and moderate and coincided with the range of classification for the values of $d$ presented. The significance level was set at 5%, and the power was 95%. The calculations indicated a total of 54 participants using the VAS and 72 participants using the WOMAC questionnaire. The calculation to be considered will be based on the WOMAC questionnaire, with 24 individuals per group, making a total of 72 individuals. Considering a possible dropout rate of 20%, 29 participants should be allocated to each group; however, to facilitate calculations and randomisation, 30 participants will be allocated to each group ($n=90$).

Data management and statistical analysis
The registration of the data collected in the evaluations will be carried out through digital forms (Google Forms) and automatically stored in an electronic database in the Cloud (Google Drive), protected by a password, to ensure the security of data and participants. After completing the collections, the data will be analysed by a ‘blind’ biostatistician, without information on the identification of the groups, using SPSS software (V.24.0; SPSS).

The independent variables of interest in the study are the group (compression, sham and control) and time (preintervention (assessment 1) and postintervention (assessments 2, 3 and 4)). The dependent variables are the VAS (pain intensity), WOMAC (total score), step test (seconds), $30\,\text{s}\,\text{sit-to-stand\,test\,number\,of\,repetitions}$, and $40\,\text{m}\,\text{accelerated\,walk\,test}\,\text{speed\,in\,m/s}$. In addition, data distribution or normality, will be tested using the Kolmogorov-Smirnov test, and according to the results, parametric or non-parametric tests will be used.

Initially, descriptive analyses will be performed using measures of central tendency and dispersion: mean and SD when following a normal distribution and the median, minimum and maximum when the distribution is not normal. For normal data, two-way ANOVA with a mixed design will be the parametric test chosen for comparison between the means of the dependent variables, considering the two factors simultaneously, one from repeated measurements (preintervention and postintervention, and follow-up at 12 and 24 weeks) and another with independent samples (compression, sham and control). If significant differences were found, multiple comparison tests (post hoc) were performed to assess the differences. For the distribution of non-normal data, the possible reasons for non-normality will be verified, analysis of possible correction, and then non-parametric tests can be applied, using both repeated (time) and non-repeated (groups) comparisons with Bonferroni adjustments or similar.

A confidence level of 95% will be determined for all variables, and a significance level of 5% will be considered statistically significant. In addition, the differences between the groups will be compared with the MDCI values defined for each variable. When MDCI values are not available, Cohen’s $d$ coefficient will be calculated (effect size: $>0.8$, large; close to 0.5, moderate and $\leq0.2$, small). Finally, to preserve the benefit of randomisation, allowing the balanced distribution of prognostic factors in the compared groups and, consequently, the observed effect, an analysis by intention-to-treat will be adopted through the expectation maximisation imputation method.

Ethics and dissemination
The project was initially submitted to the Human Research Ethics Committee of the Federal University of São Carlos, São Paulo, Brazil (Plataforma Brasil), approved under number 3955692, and later submitted to the clinical trials registry (www.clinicaltrials.gov), approved with the identification: NCT04724902. Subsequently, the study activities will be conducted. Volunteers will receive a verbal and written explanation of the objectives and methodology of the study, and those who agree to participate will be required to provide written informed consent (online supplemental material 1). The participants are free to withdraw from the study at any time without prejudice toward future treatment. The results will be presented at scientific meetings and will be published in peer-reviewed journals. All publications and presentations related to this study will be authorised and reviewed by the study investigators.

DISCUSSION
Currently, KOA is one of the main causes of musculoskeletal pain and functional disability. It is known that patients with osteoarthritis have high health costs. Therefore, effective and low-cost interventions are important. High-quality evidence has already established that physical exercise improves pain levels and physical function in individuals with KOA. However, adherence to these protocols tends to reduce over time due to barriers such as worsening pain and fear of movement. Therefore, adherence is an important factor for the continuation of these exercises in the long term. Thus, using techniques that allow pain control...
can effectively ensure greater motivation to and adherence to physical exercise in the long term.

In 2009, the estimated US spending on total knee joint replacement surgery was US$28.5 billion, and healthcare costs for osteoarthritis patients were approximately US$2600 per year.\(^1\) Compression using elastic bandages or soft orthoses is a low-cost and easy-to-apply alternative and is widely accessible to the population with knee disorders.\(^2\) Although compression is used to control pain in KOA,\(^3\) to the best of our knowledge, this is the first study that seeks to understand the isolated effect of compression on pain and physical function.

The possible mechanism of action of compression by elastic bandages in relieving pain can be explained by the theory of the gates of Melzack and Wall,\(^4\) according to which pain can be modulated by the stimulation of tactile receptors in the skin. According to the authors, a tactile stimulus, such as compression, is identified by mechanoreceptors in the skin and conducted to the spinal cord through myelinated \(\alpha\)-type afferent fibres.\(^5\) In contrast, painful stimuli from nociceptors are conducted in the spinal cord by unmyelinated fibres of type C.\(^6\) In this way, the proportion of tactile impulses that would reach the spinal cord would be higher because of the stimulation that is taking place and its higher conduction velocity. Faced with the competition for simultaneous stimulation that is taking place and its higher conduction velocity, the proportion of tactile impulses that would reach the spinal cord would be higher, because of the stimulation that is taking place and its higher conduction velocity. In this way, the proportion of tactile impulses that would reach the spinal cord would be higher, because of the stimulation that is taking place and its higher conduction velocity. In addition, aspects such as improved proprioception may be present and promote beneficial functional effects, such as better stability during movement.\(^7\)

To minimise the blinding limitation of the interventional therapist and volunteers—blinding made impossible by the physical nature of the intervention and ethical issues—we used subjective,\(^8\)\(^9\)\(^10\)\(^11\) and objective,\(^12\)\(^13\)\(^14\)\(^15\)\(^16\)\(^17\) outcome measures of physical function by blinded assessors.\(^18\)\(^19\)\(^20\) In this way, the proportion of tactile impulses that would reach the spinal cord would be higher, because of the stimulation that is taking place and its higher conduction velocity. Faced with the competition for simultaneous stimuli (tactile and painful), there would be a modulation of the conduction of nociceptive impulses and a reduction in the central perception of pain.\(^21\)\(^22\)\(^23\)\(^24\)\(^25\) In addition, aspects such as improved proprioception may be present and promote beneficial functional effects, such as better stability during movement.\(^26\)\(^27\)\(^28\)

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