ABSTRACT

Introduction Microcurrent therapy (MCT) is a rising conservative treatment for patients with knee osteoarthritis (OA). Considering its potential benefits and convenience, MCT’s application in those individuals with knee OA is capacious. However, no plausible clinical evidence has proved its unequivocal advantages in treating knee OA conservatively. The purpose of this study is to determine whether MCT is helpful in pain management and promoting function of knee OA and is safe in the treatment of knee OA in adult patients.

Methods and analysis We will search through MEDLINE, Embase, Cochrane Library, Web of Science and Google Scholar from inception to 15 March 2023. Original studies will include randomised controlled trials of patients treated with MCT. Two authors will independently screen, select studies, extract data and perform risk of bias assessment. Data consistently reported across studies will be pooled using random-effects meta-analysis. Heterogeneity will be evaluated using Cochrane’s Q statistic and quantified using I² statistics. Graphical and formal statistical tests will be used to assess for publication bias.

Ethics and dissemination Ethical approval will not be needed for this study as the data will be extracted from already published studies. The results of this review will be published in a peer-reviewed journal and presented at conferences.

PROSPERO registration number CRD42022319828

INTRODUCTION

Osteoarthritis (OA) is the most common joint disease and one of the most prominent pathological factors of disability worldwide. Knee OA affected an estimated 654 million individuals in 2020, requiring significant financial support globally. The morbidity of knee OA has a significant impact on quality of daily life and is closely associated with age, sex and financial input in China.

Knee OA is primarily a degenerative and progressive disease that mainly affects the elderly and is caused by the loss of articular cartilage. Divided into primary and secondary categories, the degeneration of articular cartilage is the major aetiology of both types. Primary knee OA is commonly attributed to age and molecular deregangement, whereas secondary knee OA is linked to a variety of known factors, including trauma, surgery, malalignment, rheumatoid arthritis and rickets. The absence of cartilage support would probably result in impeded knee flexion and extension, often accompanied by pain and other symptoms.

Knee, which comprises the femur, tibia, patella, synovium, ligaments, peri-articular fat and muscles, is susceptible to OA due to multiple factors. In the early stage of knee OA, cartilage degradation is predominantly mediated by angiogenesis, the tissue inhibitor of metalloproteinase (TIMP)/matrix metalloproteinase (MMP)/transforming growth factor (TGF) system and fat tissue metabolism. These cytokines play a role in tissue remodelling and catabolic activities, leading to the upregulation of tissue-degrading enzymes, which disrupt the structural stability and functional equilibrium of the joint. As age increases, abnormal tissue metabolism contributes to cartilage consumption. Thus,
repairing cartilage is essential to maintain joint function. However, cartilage restoration requires proper metabolism and nutrients, which may be hindered by an insufficient blood supply in the articular cartilage. The restricted joint motion, along with pain, stiffness and muscle weakness, would probably lead to inactivity. Daily activities could reduce pain, improve physical function and enhance the surrounding muscles to support joint loading. Conversely, physical inactivity may exacerbate obesity, which in turn accelerates the degradation of knee OA.

Microcurrent therapy (MCT) is a therapeutic intervention that employs low-intensity electrical currents, not exceeding 1 mA, to modulate the constant direct current flow of neural tissues. It has two output channels (A and B), each channel containing a pair of adhesive gel electrodes. Proper electrode placement involves positioning the two electrodes of each channel opposite each other, with the line of each channel (A1-A2, B1-B2) perpendicular to one another. The apparatus generates rectangular waves and switches the polarity into the opposite direction every 2.5 s. MCT is being applied clinically as a non-surgical modality for treating knee OA at present.

Clinical treatment of knee OA can be categorised as either non-surgical or surgical. The former includes strengthening, aerobic exercise, weight loss and education, which are currently considered appropriate or strongly recommended. However, the process of these methods could be relatively challenging and painful, especially for patients with moderate to severe pain. Chronic OA pain could distract them from training and exercising through anxiety, depression and fear of movement. Preferred pharmacological therapies are helpful in pain relief, but would not be as durable as non-pharmacological therapies, and dosage instructions are essential. Transcutaneous electrical nerve stimulation (TENS), a widely investigated electrotherapy, has not been recommended due to inconclusive clinical evidence and its ability to reduce pain only by inhibiting nociceptor activity. In contrast, MCT has been suggested to be beneficial for pain management and function improvement. The animal experiment has implied its efficacy of skeletal muscle recovery through muscle protein synthesis. External stress has been shown to interfere with the proliferation of satellite cells, which regenerate and restore skeletal muscle tissues after injury. In vitro experiments have shown MCT accelerates the recovery of injured skeletal muscles. Several pieces of research have reported the beneficial effects of MCT, including pain relief, function improvement, wound healing and less irritation. When integrated with traditional treatment, MCT has been shown to provide better outcomes than traditional treatment alone. A recent clinical trial demonstrated the pain-reducing effect of MCT in knee OA. However, it did not show significant improvement in knee function. MCT has also shown the superiority of conventional therapies in certain aspects.

Given the increasing recognition of MCT as a potential alternative clinical approach for knee OA, it is imperative to obtain rigorous evidence for clinicians. To the best of our knowledge, there has been no systematic review and meta-analysis on this topic. Therefore, we have undertaken this study to estimate the clinical effects of MCT in treating knee OA, with the aim of determining its efficacy in pain management and promoting knee function, as well as evaluating its safety in adult patients.

RESEARCH AIMS
This study aims to examine the clinical efficacy of MCT for patients diagnosed with knee OA worldwide.

PROTOCOL AND REGISTRATION
This protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) on 23 April 2022. The protocol was reported following the Preferred Reporting Items for Systematic Review and Meta-analysis Protocols statement. The relevant systematic review and meta-analysis will also be reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.

METHODS
Patient and public involvement
Patients and the public were not involved.

Eligibility criteria
All clinical studies that cater to the following inclusion criteria will be included:
1. Randomised controlled trials focus on the clinical effects of MCT on knee OA in adults.
2. Age: The participants should not be younger than 18 years old.
3. Language: There is no language restriction.
4. Duration: We will recruit all studies from inception to 15 March 2023 in several databases.
5. Sample size restriction: There is no sample size restriction.

The following will be the exclusion criteria:
1. Non-comparative clinical studies, studies without required clinical outcomes (Visual Analogue Scale (VAS) Score, Range of Motion (ROM), Knee Injury and Osteoarthritis Outcome Score (KOOS)/Knee Injury and Osteoarthritis Outcome Score-Physical Function Short-form (KOOS-PS)/Oxford Knee Score (OKS)/Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index), studies that used TENS instead of MCT.
2. Studies whose clinical data cannot be fully accessed after contact with authors.
3. Case reports, literature reviews, technical notes and editorial comments.
4. Cadaveric studies, animal experiments.
Table 1: The search strategy used in Embase with each search term

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</table>

Search strategy

Original studies will be searched through MEDLINE, Embase, Cochrane Library, Web of Science and Google Scholar from inception to 15 March 2023. Search keywords will be: ‘microcurrent therapy’, ‘electrotherapy’, ‘knee osteoarthritic’, ‘knee osteoarthrosis’. We would use vocabulary synonyms to search related original studies. The search strategy is demonstrated in table 1.

After inputting original studies into EndNote V.X9, two reviewers (YXX and YZ) will, independently and in duplicate, screen the titles and abstracts of all studies to generate a list of eligible trials from which full texts could be obtained. Afterwards, reviewers will independently assess the eligibility of these full texts of published trials and search the reference lists of these publications to decide on the final included studies.

Discrepancies will be resolved through discussion or arbitrated by a third reviewer (ZLZ) if necessary to make the final decision.

Data extraction

Two investigators (YZ and YXX) will independently extract data from included studies using a standardised and pretested data extraction form. Following data will be extracted as study characteristics: authors, country of origin, year of publication, the study design, sample size, the mean or median age of the population, gender, severity of knee OA, follow-up, the mean or median duration of MCT, randomisation, blinding, allocating concealment, primary outcomes and adverse events. Any potential discrepancies will be arbitrated by a third investigator (ZLZ).

Methodological appraisal

Two authors (ZLZ and YXX) will assess the quality of eligible studies guided by the Cochrane Handbook for Systematic Reviews of Interventions (V.6.3, 2022).

DATA ANALYSIS

All data will be analysed using the RevMan software (V.5.4.1). Interobserver agreement for study inclusion will be assessed using Cohen’s κ coefficient. A narrative description will be provided when data are unable to conduct a meta-analysis. These data will include study characteristics such as year of publication, follow-up times, sample size and clinical outcomes. The recovery of knee OA will be reported in terms of pain and function. Random-effects model meta-analyses will be used to pool estimates across studies for the outcomes of interest. Heterogeneity across studies will be evaluated using Cochrane’s Q statistic and quantified using I² statistics. Where substantial heterogeneity is detected, a subgroup analysis will be performed to explore the possible sources using the following grouping variables: age group, gender, frequency and intensity of intervention, and study quality. Cochrane Collaboration criteria will be used to assess the risk of bias (including seven items of selection bias, performance bias, detection bias, attrition bias, reporting bias and other forms of bias). Graphical and formal statistical tests will be used to assess for publication bias. Potential outliers will be investigated in a sensitivity analysis by dropping each study at a time. The Duval and Tweedie trim-and-fill will be used to adjust estimates for the effects of publication bias. The primary outcome is the VAS variation and the score calculated from the instruments of knee function. The original scores will be converted into 0–100 point scales, then the alteration of the points from baseline to the end of treatment will be examined.

ETHICS AND DISSEMINATION

Due to the characteristics of this study design, ethical evaluation was not required. The findings of this systematic review will be disseminated through peer-reviewed publications and presented at international conferences related to this field.

Contributors ZLZ and YXX contributed equally to this article. ZLZ registered the protocol in the PROSPERO database. YXX conducted the database search strategy. YZ and XHM conducted the data extraction and analysis plan. ZLZ and YXX wrote the manuscript draft. LX amended the draft. All authors read, revised and approved the final manuscript.

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Competing interests None declared.
Patient and public involvement  Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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REFERENCES