Study Protocol Systematic Review

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Effectiveness of electrical stimulation for postoperative pain in patients with osteosarcoma

A systematic review protocol of clinical controlled trial

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Abstract

Background: This study aims to investigate the effectiveness and safety of electrical stimulation (ES) for postoperative pain (PPP) in patients with osteosarcoma systematically.

Methods: We will systematically search the following electronic databases from inception to the May 1, 2019: MEDILINE, Cochrane Library, EMBASE, Web of Science, Springer, and CNKI without language restrictions. All literatures of randomized controlled trials (RCTs) and case-controlled studies (CCSs) of ES for PPP in patients with osteosarcoma will be included. RevMan 5.3 software (Cochrane Community; London, UK) and STATA 15.0 software (StataCorp; College Station) will be used for statistical analysis. Cochrane risk of bias will be used for methodological quality assessment for RCTs and Newcastle-Ottawa Scale will be utilized for CCSs.

Results: This study will assess the clinical effectiveness and safety of ES for PPP in patients with osteosarcoma through assessing primary outcome of pain intensity and secondary outcomes of frequency of rescue analgesic use, cumulative morphine consumption, quality of recovery, as well as adverse events.

Conclusion: This study will provide latest evidence on effectiveness and safety of ES for PPP in patients with osteosarcoma, and may also provide guidance for both clinician and further studies.

Dissemination and ethics: This study does not require ethical approval, because it will not analyze the individual patient data. Its results are expected to be published in peer-reviewed journals.

Systematic review registration: PROSPERO CRD42019135790.

Abbreviations: CCSs = case-controlled studies, CIs = confidence intervals, ES = electrical stimulation, PPP = postoperative pain, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analysis, RCTs = randomized controlled trials.

Keywords: effectiveness, electrical stimulation, osteosarcoma, postoperative pain, safety

1. Introduction

Osteosarcoma is the most common type of bone cancer in children and teenagers.[1–3] Previous studies have reported that the incidence rate of osteosarcoma is 4 to 5 patients per 1,000,000 persons.[4,5] Other studies have reported that its 5-year overall survival rate and 5-year disease-free survival rate are about 50% to 60% and 40%, respectively.[6–8] The huge amount cost of treatment and care also brings heavy burden for both families and society.[9,10]

Currently, although a variety of therapies for this condition has been reported, the efficacy is still not satisfied.[11–13] These therapies mainly include medications and surgery.[14,15] Though many patients choose surgery for their treatment, it also accompanies a lot of complications, such as postoperative pain (PPP), infection, and so on.[16,17]

Electrical stimulation (ES) has been reported to treat a variety of pain conditions effectively and safety.[18–23] Furthermore, many studies also reported to use ES for the treatment of PPP in patients with osteosarcoma.[24–26] However, no study has systematically assessed its effectiveness and safety for PPP. Thus, this study will investigate the effectiveness and safety of ES for osteosarcoma patients with PPP.

2. Methods

2.1. Objective

The aim of this study is to investigate the effectiveness and safety of ES for osteosarcoma in patients with PPP.

2.2. Study registration

We have registered this study on http://www.crd.york.ac.uk/PROSPERO with CRD42019135790. It has been designed and reported according to the guidelines of the Preferred Reporting

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Items for Systematic Reviews and Meta-Analysis (PRISMA) Protocol statement.[27]

2.3. Inclusion criteria for study selection

2.3.1. Type of study. We will include all randomized controlled trials (RCTs) and case-controlled studies (CCSs) of ES for PPP in patients with osteosarcoma. However, animal studies, reviews, case studies, and non-case CCSs will all be excluded.

2.3.2. Type of participants. All osteosarcoma participants with PPP will be included without any limitations of age, sex, and race.

2.3.3. Type of interventions. The patients in experimental group must be treated with any forms of ES, such as electrical muscle stimulation, Russian ES, neuromuscular ES, functional ES, and transcutaneous electrical nerve stimulation.

The participants in the control group have been treated with any non-ES therapies.

2.3.4. Type of outcome measurements. The primary outcome of pain intensity can be measured by Numerical Rating Scale, or any other pain scales. The secondary outcomes can be measured by the frequency of rescue analgesic use, cumulative morphine consumption, and quality of recovery. The dose, frequency of all analgesic will be monitored and recorded during the period of hospital stay. The cumulative morphine consumption will also be documented during the period of hospital stay. The quality of recovery will be measured by the Quality of Recovery-9 or other relevant scales, which is used to evaluate the patient's quality of recovery after anesthesia. In addition, any adverse events will also be assessed.

2.4. Search methods for the identification of studies

2.4.1. Electronic searches. The following databases will be systematically searched from inception to the May 1, 2019: MEDILINE, Cochrane Library, EMBASE, Web of Science, Springer, and CNKI without language restrictions. The search details for MEDLINE are demonstrated in Table 1. The equivalent strategies will be used to any other electronic databases.

2.4.2. Search for other resources. In addition, any clinical registry websites, dissertations, and reference lists of relevant reviews will be searched to avoid missing any potential studies.

Table 1

Search strategy for MEDLINE database.

Number	Search terms
1	osteosarcoma
2	osteogenic sarcoma
3	bone cancer
4	bone tumor
5	Or/1-4
6	pain
7	pain, postoperative
8	postoperative
9	post surgery
10	pain intensity
11	Or/6–10
12	randomized controlled trial
13	case-controlled studies
14	case studies
15	controlled study
16	randomly
17	randomized
18	placebo
19	sham
20	trial
21	Or/12–20
22	electrical stimulation
23	electric stimulation
24	therapy
25	treatment
26	intervention
27	modalities
28	electrical muscle stimulation
29	functional electrical stimulation
30	Or/20–29
31	5 and 11 and 21 and 30

2.5. Data collection and analysis

2.5.1. Study selection. Two reviewers will independently operate all literature selection according to the predefined study selection eligibility. In case of any disagreements regarding the study selection between 2 reviewers, a third reviewer will take part in to help solve them by discussion. There are 2 stages for all literature selection. At first stage, the titles and abstracts of all literatures will be checked, and irrelevant literatures will be excluded. At the second stage, all remaining literatures will be read by full-text to further determine if they meet all eligibility criteria. The process of 2-stage study selection will be presented in the PRISMA flow chart.

2.5.2. Data extraction and management. Two reviewers will independently carry out data extraction according to the PRISMA flowchart and pre-designed eligibility criteria. The extracted information comprises of title, authors, year of publication, location, study design, sample size, study methods, intervention details, outcome measurements, and adverse events. Any divergences between 2 reviewers will be settled down by a third reviewer through discussion.

2.5.3. Missing data management. For any insufficient or missing, or unclear data, we will contact original corresponding authors to obtain them. If we can not achieve them, only available data will be analyzed in this study.

2.5.4. Methodological quality assessment. Two reviewers will independently assess the methodological quality for each eligible study. Any disagreements between 2 reviewers will be resolved by a third reviewer through discussion. For RCTs, their methodological quality will be measured by Cochrane risk of bias tool. For CCSs, their methodological quality will be assessed by Newcastle-Ottawa Scale.

2.6. Statistical analysis

2.6.1. Measurement of treatment effect. The continuous data will be shown with mean difference or standardized mean difference and 95% confidence intervals (CIs). The dichotomous data will be performed with odd ratio or risk ratio and 95% CIs.

2.6.2. Assessment of heterogeneity. The test of I^2 will be utilized to detect the heterogeneity among eligible studies. A fair heterogeneity is defined as $I^2 \leq 50\%$. On the other hand, significant heterogeneity is defined as $I^2 > 50\%$.

2.6.3. Data synthesis. If $I^2 \leq 50\%$, the outcome data will be synthesized by a fixed-effect model. In addition, we will also carry out meta-analysis if it is possible. Otherwise, if $I^2 > 50\%$, the outcome data will be synthesized by a random-effect model. At the same time, we will also conduct subgroup analysis to find any factors that may lead to high heterogeneity. If significant heterogeneity is still detected after subgroup analysis, outcome data will not be synthesized, and meta-analysis will not be performed. Instead, we will report outcome results using narrative summary description.

2.6.4. Subgroup analysis. Subgroup analysis will be carried out according to the different forms of treatments, controls, and outcomes.

2.6.5. Sensitivity analysis. We will carry out sensitivity analysis to check the robustness of the pooled results based on the different methodological quality and statistical models.

2.6.6. Publication bias. If this study includes >10 eligible studies, we will carry out funnel plot[28] and Egger test to check if there is publication bias in this study.[29]

3. Discussion

PPP is gravely tormenting patients and greatly reduces their quality of life. A variety of clinical studies have reported ES can help to treat PPP in patients with osteosarcoma.[24–26] Thus, in this study, we will comprehensively search more potential literatures and will systematically evaluate the effectiveness and safety of ES for osteosarcoma patients with PPP. The results of this study will summarize the updated evidence on the effectiveness and safety of ES for osteosarcoma patients with PPP. It may also provide beneficial evidence for the clinical practice and health policy-makers.

Author contributions

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References

[1] Kebudi R, Ozger H, Kızılocak H, et al. Osteosarcoma after hematopoietic stem cell transplantation in children and adolescents: case report and review of the literature. Pediatr Blood Cancer 2016;63:1664–6.
[2] Rogozhin DV, Bulycheva IV, Konovalov DM, et al. Classical osteosarcoma in children and adolescent. Arkh Patol 2015;77:68–74.
[3] Fayda M, Kebudi R, Dizdar Y, et al. Spontaneous pneumothorax in children with osteosarcoma: report of three cases and review of the literature. Acta Chir Belg 2012;112:378–81.
[4] Taran SJ, Taran R, Malipatil NB. Pediatric osteosarcoma: an updated review. Indian J Med Paediatr Oncol 2017;38:33–43.
[5] Geller DS, Gorlick R. Osteosarcoma: a review of diagnosis, management, and treatment strategies. Clin Adv Hematol Oncol 2010;8:705–18.
[6] Wan J, Zhang X, Liu T, et al. Strategies and developments of immunotherapies in osteosarcoma. Oncol Lett 2016;11:511–20.
[7] Hansen MF, Seton M, Merchant A. Osteosarcoma in Paget's disease of bone. J Bone Miner Res 2006;21(suppl):58–63.
[8] Chakravarty K, Saeed IT, Fowler RW. A fatal case of pleural osteosarcoma mimicking mesothelioma in Paget's disease of bone. Rheumatology (Oxford) 2003;42:1578–9.
[9] Cornelio N, Burudpakdee C. A guideline-based estimate of health care resource use and cost of metastatic unresectable osteosarcoma. Value Health 2014;17:A629–30.
[10] Brosa M, García del Muro X, Mora J, et al. Orphan drugs revisited: cost-effectiveness analysis of the addition of mifamurtide to the conventional treatment of osteosarcoma. Expert Rev Pharmacoecon Outcomes Res 2015;15:331–40.
[11] ElKordy MA, ElBaradie TS, ElSebai HI, et al. Osteosarcoma of the jaw: challenges in the diagnosis and treatment. J Egypt Natl Canc Inst 2018;30:7–11.
[12] Niu XH. Standardized diagnosis and treatment of osteosarcoma in China is imperative. Zhonghua Zhong Liu Za Zhi 2013;35:161–3.
[13] Piperno-Neumann S. Diagnosis and treatment of primary osteosarcoma in 2009. Bull Cancer 2010;97:715–21.
[14] Wittig JC, Bickels J, Priebat D, et al. Osteosarcoma: a multidisciplinary approach to diagnosis and treatment. Am Fam Physician 2002;65:1123–32.
[15] Papagelopoulos PJ, Galanis EC, Vlastou C, et al. Current concepts in the evaluation and treatment of osteosarcoma. Orthopedics 2000;23:858–67.
[16] Mei J, Ni M, Jia GY, et al. Intermittent internal fixation with a locking plate to preserve epiphyseal growth function during limb-salvage surgery in a child with osteosarcoma of the distal femur: a case report. Medicine (Baltimore) 2015;94:e830.
[17] Kohyama K, Yamada K, Sugiura H, et al. Salvage surgery and microsurgical reconstruction for recurrence of skull base osteosarcoma after carbon ion radiotherapy. Nagoya J Med Sci 2015;77:667–73.
[18] Guo P, Wang JW, Tong A. Therapeutic effectiveness of neuromuscular electrical stimulation for treating patients with chronic low back pain. Medicine (Baltimore) 2018;97:e13197.
[19] Chen FC, Shao HL, Han FL. A pilot study of neuromuscular electrical stimulation for neuropathic pain caused by spinal cord injury. Medicine (Baltimore) 2018;97:e11658.
[20] Li YP, Cui X, Liu SC, et al. Neuromuscular electrical stimulation for treating postpartum low back pain. Medicine (Baltimore) 2018;97:e11426.
[21] Bi XL, Xie CX. Effect of neuromuscular electrical stimulation for endometriosis-associated pain: a retrospective study. Medicine (Baltimore) 2018;97:e11266.
[22] Miao Q, Qiang JH, Jin YL. Effectiveness of percutaneous neuromuscular electrical stimulation for neck pain relief in patients with cervical spondylosis. Medicine (Baltimore) 2018;97:e11080.
[23] Martimbianco ALC, Torloni MR, Andriolo BN, et al. Neuromuscular electrical stimulation (NMES) for patellofemoral pain syndrome. Cochrane Database Syst Rev 2017;12:CD011289.
[24] Castellano JJ, Rojas AM, Karia R, et al. A randomized, double-blind, placebo-controlled study of neuromuscular electrical stimulation (NMES) use for recovery after elective total hip replacement surgery. Bull Hosp Jt Dis (2013) 2016;74:275–81.
[25] Volpato HB, Szego P, Lenza M, et al. Femoral quadriceps neuromuscular electrical stimulation after total knee arthroplasty: a systematic review. Einstein (Sao Paulo) 2016;14:77–98.
[26] Broderick BJ, Breathnach O, Condon F, et al. Haemodynamic performance of neuromuscular electrical stimulation (NMES) during recovery from total hip arthroplasty. J Orthop Surg Res 2013;8:3.
[27] Shamseer L, Moher D, Clarke M, et al. PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015;350:g7647.
[28] Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration; 2011. Available at: http://www.cochrane-handbook.org. Accessed April 10, 2019.
[29] Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629–34.