INPLASY PROTOCOL

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Review Stage at time of this submission: **The review has not yet started.**

Conflicts of interest:
None.

Neuromuscular electrical stimulation for cancer pain in children with osteosarcoma: A protocol of systematic review

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Review question / Objective: **Is neuromuscular electrical stimulation (NMES) effective and safe for cancer pain (CP) in children with osteosarcoma?**
Condition being studied: **Neuromuscular electrical stimulation; cancer pain; osteosarcoma.**
Information sources: **The following electronic databases will be systematically retrieved from inception to June 1 in Cochrane Library, MEDLINE, EMBASE, Web of Science, Scopus, CNKI and VIP database. We will also carry out manual head-searching of reference lists and conference proceedings to avoid missing potential articles. The search strategy will not restrict to any language and publication status. The proposed MEDLINE search strategy with details is created. The similar search strategy will be adapted to the other electronic databases. The search strategy will be carried out in conjunction with a research librarian who is an expert in systematic reviews. Additionally, we will carry out head-searching of reference lists and conference proceedings.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 June 2020 and was last updated on 14 June 2020 (registration number INPLASY202060054).

INTRODUCTION

Review question / Objective: **Is neuromuscular electrical stimulation (NMES) effective and safe for cancer pain (CP) in children with osteosarcoma?**

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METHODS

Participant or population: **Participants (under 18 years old) with confirmed CP in**

children with osteosarcoma will be included without restrictions to ethnicity, sex, and characteristics of osteosarcoma.

Intervention: Experimental group: all patients received any types of NMES.

Comparator: Control group: all patients received any interventions, but not any forms of NMES.

Study designs to be included: We will include randomized controlled trials (RCTs) that assessed the effectiveness and safety of NMES for CP in children with osteosarcoma.

Eligibility criteria: We will include RCTs that assessed the effectiveness and safety of NMES for CP in children with osteosarcoma. We will exclude other studies, such as non-clinical trial, uncontrolled trials, and non-RCTs.

Information sources: The following electronic databases will be systematically retrieved from inception to June 1 in Cochrane Library, MEDLINE, EMBASE, Web of Science, Scopus, CNKI and VIP database. We will also carry out manual head-searching of reference lists and conference proceedings to avoid missing potential articles. The search strategy will not restrict to any language and publication status. The proposed MEDLINE search strategy with details is created. The similar search strategy will be adapted to the other electronic databases. The search strategy will be carried out in conjunction with a research librarian who is an expert in systematic reviews. Additionally, we will carry out head-searching of reference lists and conference proceedings.

Main outcome(s): The primary outcome is pain intensity, as assessed by any pain scales in the reported trials. The secondary outcomes are frequency of rescue analgesic utilization, cumulative anesthetic drug administration, quality of life, and adverse events.

Data management: Two authors will independently collect data using a previously defined data collection form. Any disagreements will be solved by a third author through discussion. The collected data include descriptive information (e.g. study reference, study objective, trial design, title, first author, and geographic location), study population (e.g. diagnostic criteria, inclusion and exclusion criteria, demographic characteristics, and sample size), study methods (e.g. randomization details, blind, and concealment), intervention details (e.g. dosage, duration, and deliver methods), outcome indicators, follow-up information, study results, findings, and conflict of interest.

Quality assessment / Risk of bias analysis: Two authors will independently examine risk of bias using Cochrane Risk of Bias Tool. It covers seven aspects, and each one is divided into three levels: low risk of bias, unclear risk of bias, and high risk of bias. Any confusion will be cleared up by a third author through discussion.

Strategy of data synthesis: We will carry out RevMan 5.3 software using statistical analysis. All continuous data will be estimated as mean difference (MD) or standardized MD with 95% confidence intervals (CIs). All dichotomous data will be estimated as risk ratio with 95% CIs. Statistical heterogeneity will be examined using I^2 statistics. It is defined as follows: $I^2 \leq 50\%$ exerts acceptable heterogeneity, and we will use a fixed-effect model. $I^2 > 50\%$ means significant heterogeneity, and we will utilize a random-effect model. Meta-analysis will be conducted when the eligible trials are sufficiently homogenous in terms of study design, patient characteristics, details of interventions and controls, and outcome indicators. If meta-analysis is inappropriate, we will report study results by descriptive analysis.

Subgroup analysis: Subgroup analysis will be carried out to check the possible sources that may cause significant heterogeneity according to the different study information, participant characteristics, details of intervention and control, and study quality.

Sensibility analysis: Sensitivity analysis will be performed to test the robustness of study findings by removing low quality studies.

Country(ies) involved: China.

Keywords: Osteosarcoma; neuromuscular electrical stimulation; cancer pain; effectiveness.

Contributions of each author:
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Author 2 - Shou-feng Wang.
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