INPLASY PROTOCOL

To cite: Jiang et al. Gabapentin for phantom limb pain after amputation in pediatric oncology: a systematic review protocol. Inplasy protocol 202060090. doi: 10.37766/inplasy2020.6.0090

Received: 23 June 2020

Published: 24 June 2020

Corresponding author:
Li-hua Yan

Li-huaYan2001@outlook.com

Author Affiliation:
Cancer Hospital of China Medical University

Support: **Not applicable.**

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

Conflicts of interest:
None.

Gabapentin for phantom limb pain after amputation in pediatric oncology: a systematic review protocol

Jiang, S[1]; Zhou, MM[2]; Xia, R[3]; Bai, JH[4]; Yan, LH[5].

Review question / Objective: **1. Does gabapentin relieve phantom limb pain (PLP) after amputation in pediatric oncology? 2. Is gabapentin safe for the treatment of PLP after amputation in pediatric oncology?**
Condition being studied: **Phantom limb pain; amputation; gabapentin.**
Information sources: **We will systematically retrieve electronic databases (Cochrane Library, MEDLINE, EMBASE, Web of Science, CINAHL, PsychINFO, Scopus, WANGFANG, and Chinese Biomedical Literature Database) from the inception to the present without restrictions to publication status and language. A search strategy for Cochrane Library with details is presented. Similar search strategies for other electronic databases will be adapted and applied. Translations will be performed when necessary. At the same time, we will examine unpublished and ongoing work in clinical trial registry, conference proceedings, and reference lists of eligible trials.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 June 2020 and was last updated on 24 June 2020 (registration number INPLASY202060090).

INTRODUCTION

Review question / Objective: **1. Does gabapentin relieve phantom limb pain (PLP) after amputation in pediatric oncology? 2. Is gabapentin safe for the treatment of PLP after amputation in pediatric oncology?**

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METHODS

Participant or population: **Pediatric population (under 18 years old) with**

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confirmed of bone cancers, received chemotherapy before limb amputation and suffered from PLP, irrespective of race, sex, and duration of PLP.

Intervention: In the experimental group, all participants received gabapentin for PLP after amputation in pediatric oncology.

Comparator: In the control group, all subjects received other treatments (such as placebo, sham comparator) for PLP after amputation in pediatric oncology.

Study designs to be included: Randomized controlled trials (RCTs) and case-controlled studies (CCSs) of gabapentin compared with other treatments (such as placebo, sham comparator).

Eligibility criteria: Inclusion criteria Inclusion criteria of this study are: 1) randomized controlled trials (RCTs) and case-controlled studies (CCSs) of gabapentin compared with other treatments (such as placebo, sham comparator) for PLP after amputation in pediatric oncology; 2) studies disseminated up to the present in any language and publication status; 3) pediatric population (under 18 years old) with confirmed of bone cancers, irrespective of race, sex, and duration of PLP; 4) eligible participants who received chemotherapy before limb amputation and suffered from PLP; and 5) studies report one of the outcomes of interest. Exclusion criteria Exclusion criteria of this study are: 1) participants with multiple metastatses, abnormal renal and hepatic function, and allergic to gabapentin and study drugs; 2) pain caused by other diseases; and 3) studies of animal study, review, editorial letter, case report, case series, non-clinical trial, and uncontrolled study.

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Main outcome(s): Primary outcome - Pain intensity (any pain scale reported in the trial, such as visual analogue scale). Secondary outcome - Analgesic drug consumption (any analgesic medication reported in the trial); Sleep quality (any related scale reported in the trial, such as Medical Outcomes Study Sleep Scale); Depression (any associated score reported in the trial, such as Zung Depression Scale); Anxiety (any relevant tool reported in the trial, such as Beck Anxiety Inventory); Health-related quality of life (any relevant tool reported in the trial, such as 36-Item Short Form Survey); and Adverse events (any records reported in the trial).

Data management: Data from selected RCTs and CCSs will be transferred from their original presentation to a standard form with each included study receiving a reference code. If necessary, we will also extract indirect data from figures and charts. For all included RCTs and CCSs, two authors will independently obtain the data from eligible trials according to the predefined data extraction sheet developed specifically for this study. Any opposite views regarding the data extraction will be resolved by discussion with the help of another author. The extracted information consists of study characteristics (such as country, title, language, publication time, and funding source), patient characteristics (such as age, gender, and diagnostic criteria), study design (such as randomization details, blind, and lost to follow up), intervention and control details (such as treatment types, duration, and number and length of sessions), outcomes, safety, and other related information, such as confounding factors.

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Quality assessment / Risk of bias analysis: Study quality of each eligible study will be examined by two independent authors using Cochrane Collaboration's Risk of Bias Tool for RCTs and Newcastle-Ottawa Scale for CCSs, with predetermined criteria. RCTs will be assessed on seven aspects and each one is further rated as high, unclear or low risk of bias. CCSs will be appraised on three broad perspectives with eight specific items. Any doubt between two authors will be answered with a third author through discussion.

Strategy of data synthesis: We will use RevMan 5.3 software to synthesize and analyze outcome data. We will calculate the treatment effect of dichotomous data using risk ratio and 95% confidence intervals (CIs), and that of continuous data using mean difference (MD) or standardized MD and 95% CIs. We will examine heterogeneity using I^2 statistic, and we will undertake statistical pooling on groups of trials which are considered to be sufficiently similar. Where heterogeneity is low or minor (I^2 ≤25%), we will utilize a fixed-effect model to pool the data; if heterogeneity is moderate (25% < I^2 ≤75%), we will apply a random-effect model to synthesize the data; and if heterogeneity is obvious (I^2 >75%), we will not pool the data [40]. Meta-analysis will be carried out based on the sufficient homogeneity regarding on participant characteristics, types of intervention and outcome, and comparability between methods and ability to aggregate data. A narrative synthesis of eligible trials will be performed if the extracted data is too diverse to fulfill the threshold for meta-analytic approach. We will build a 'summary of findings' table for the outcomes and we will appraise evidence quality of primary outcome using Grading of Recommendations Assessment, Development and Evaluation, which covers five aspects of risk of bias, imprecision, consistency of effect, indirectness and publication bias.

Subgroup analysis: We will carry out subgroup analysis to test the sources of significant heterogeneity based on the different geographical regions, time periods, study quality, and types of intervention and control.

Sensibility analysis: We will investigate the sensitivity analysis to test the stability and robustness of study findings based on the sample size of included trials, and study quality.

Country(ies) involved: China.

Keywords: Phantom limb pain; amputation; gabapentin; efficacy; safety.

Contributions of each author:
Author 1 - Shuang Jiang.
Author 2 - Meng-meng Zhou.
Author 3 - Rong Xia.
Author 4 - Jing-hui Bai.
Author 5 - Li-hua Yan.

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