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Optimal concentration of ropivacaine for peripheral nerve blocks in adult patients: a protocol for systematic review and meta-analysis

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ABSTRACT

Introduction Ropivacaine is the most widely used local anaesthetic for peripheral nerve blocks (PNBs). The effects of various concentrations of ropivacaine in PNB have been investigated and compared by many randomised controlled trials (RCTs). This protocol aims to identify the optimal concentration of ropivacaine for PNB in adult patients.

Methods and analysis PubMed, EMBASE, the Cochrane library and Web of Science will be searched from their inception to 10 July 2023. RCTs that compare the analgesic effects of different concentrations of ropivacaine for PNB will be included. Retrospective studies, meta-analyses, reviews, case reports, letters, conference abstracts and paediatric studies will be excluded. The duration of analgesia will be named as the primary outcome. Secondary outcomes will include the onset time of motor and sensory blockade, postoperative pain scores, analgesic requirements over 24 hours and the incidence of adverse effects. The study selection, data extraction and quality assessment will be performed by two independent reviewers. Data processing and analysis will be performed by RevMan 5.4. The quality of the evidence will be assessed by the Grading of Recommendations Assessment, Development and Evaluation approach.

Ethics and dissemination Ethical approval is not applicable. The results of this study will be submitted to peer-reviewed journals.

PROSPERO registration number CRD42023406362.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Subgroup analysis will be used to explore the heterogeneity resource and provide evidence to guide ropivacaine use in certain surgical types or specific approaches to PNB.
⇒ We will use the Grading of Recommendations Assessment, Development and Evaluation approach to assess the quality of evidence for primary outcomes.
⇒ Significant heterogeneity may exist among the included randomised controlled trials due to several factors, such as the type of surgery or nerve block, the usage of general anaesthetics, opioids or adjuvants and the volumes of ropivacaine.

INTRODUCTION

Peripheral nerve blocks (PNBs) are widely used to provide perioperative analgesia for various types of surgeries.[1–3] In addition to pain relief, PNB can also reduce the consumption of general anaesthetics and/or opioids, decrease the incidence of postoperative complications and improve the recovery quality.[4–6] Currently, ropivacaine is the most commonly used local anaesthetic for PNB due to its lower toxicity in the central nervous system and heart.[7 8] The concentrations of ropivacaine used for PNB are various, and the efficacy and safety of different concentrations of ropivacaine have been compared in several RCTs,[9–14] but the results were inconsistent. Therefore, it is meaningful to perform a systematic review and meta-analysis to determine the optimal concentration of ropivacaine for PNB, which may provide longer analgesia without increasing the incidence of adverse effects. Furthermore, we will perform a subgroup analysis to find the recommended ropivacaine concentration for a specific type of nerve block.

METHODS AND ANALYSIS

Study registration

This protocol has been registered in the International Prospective Register of Systematic Reviews (PROSPERO; registration number: CRD42023406362). This study is conducted according to the Preferred Reporting Items for Systematic Evaluation and Meta-Analysis Protocols. Ethical approval is not required.

Search strategy

We will search PubMed, the Cochrane library, EMBASE and the Web of Science from their inception to 10 July 2023, to identify RCTs that compared the analgesic effects of different concentrations of ropivacaine for

Table 1 The search strategy in PubMed

Number	Search terms
#1	Ropivacaine (Mesh)
#2	Ropivacaine (title/abstract)
#3	#1 OR #2
#4	Nerve block (title/abstract)
#5	Nerve blockade (title/abstract)
#6	Peripheral nerve block (title/abstract)
#7	Peripheral nerve blockade (title/abstract)
#8	#4 OR #5 OR #6 OR #7
#9	Randomised controlled trial (title/abstract)
#10	Randomised (title/abstract)
#11	Clinical study (title/abstract)
#12	Clinical trial (title/abstract)
#13	Controlled clinical trial (Title/Abstract)
#14	#9 OR #10 OR #11 OR #12 OR #13
#15	#3 AND #8 AND #14

PNB. The keywords for the search will include 'ropivacaine', 'nerve block' and 'randomised controlled trials'. The language will be restricted to English. The search strategy for PubMed and other databases is presented in table 1 and online supplemental file 1, respectively.

Inclusion and exclusion criteria

Study type: RCTs, participants: adult patients (>18 years) who underwent surgeries with PNB, comparisons: different concentrations of ropivacaine for PNB, primary outcomes: duration of analgesia (time to first analgesic request), secondary outcomes: the onset time of motor and sensory blockade, postoperative pain scores, analgesic requirements over 24 hours, and the incidence of adverse effects (eg, nausea, vomiting, drowsiness, dizziness, itching and constipation). Retrospective studies, meta-analyses, reviews, case reports, letters and conference abstracts will be excluded.

Study selection

Two authors will independently select eligible studies by screening their title, abstract, and full text. The disagreement will be resolved by discussion with a third author. The flowchart for study selection is shown in figure 1.

Data extraction

The following information will be extracted: author, publication year, countries, sample, characteristics of participants, surgical type, type of anaesthesia and nerve blocks, adjuvants, comparisons, outcomes and perioperative analgesia.

Risk of bias assessment

We will assess the risk of bias for included studies using the Cochrane Collaboration tool.[15] Six items will be focused on random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias) and selective reporting (reporting bias). The estimated results for each item will be graded as 'unclear', 'low' or 'high'.

Statistical analysis

Data analysis will be performed by RevMan 5.4. Continuous data will be summarised using mean differences with 95% CI. Dichotomous data will be summarised by risk ratios (RR) with a 95% CI. Statistical heterogeneity will be assessed by the I^2 test. Data will be synthesised using a fixed-effect model if I^2<50%. Significant heterogeneity will be considered to exist when I^2>50%, and then a random-effects model will be applied. Subgroup analysis and meta-regression will be further conducted to explore the heterogeneity source. We will also perform a sensitivity analysis to test whether the results are robust and reliable. p<0.05 means statistically significant. The GRADE approach will assess the quality of evidence for each outcome, and the evidence will be rated as 'very low', 'low', 'moderate' or 'high'.

Patient and public involvement

None.

ETHICS AND DISSEMINATION

Ethical approval is not applicable. The results of this study will be submitted to peer-reviewed journals.

DISCUSSION

Ropivacaine is the most commonly used local anaesthetic for PNB due to its lower central nervous system and cardiac toxicity. Currently, the concentration of ropivacaine used for PNB mainly varies from 0.25% to 1%. Emerging RCTs have compared the effects of different concentrations of ropivacaine for PNB, but the optimal concentration remains unclear. This protocol for a systematic review and meta-analysis aims to identify the optimal concentration of ropivacaine for PNB in adult patients. An optimal concentration of ropivacaine will offer longer analgesia but not increase the incidence of adverse effects. However, several limitations should be noticed. First, significant heterogeneity may exist among the included RCTs due to several factors, such as the type of surgery or nerve block, the usage of general anaesthetics, opioids or adjuvants and the volumes of ropivacaine. Second, it should be considered that the definition of the duration of analgesia among studies may be different, which will influence the results. It is better to minimise the heterogeneity by categorising the analgesia duration differently according to their definition in individual studies. Therefore, we will use subgroup analysis and meta-regression to explore the source of heterogeneity. We will also perform a sensitivity analysis to test whether the pooled

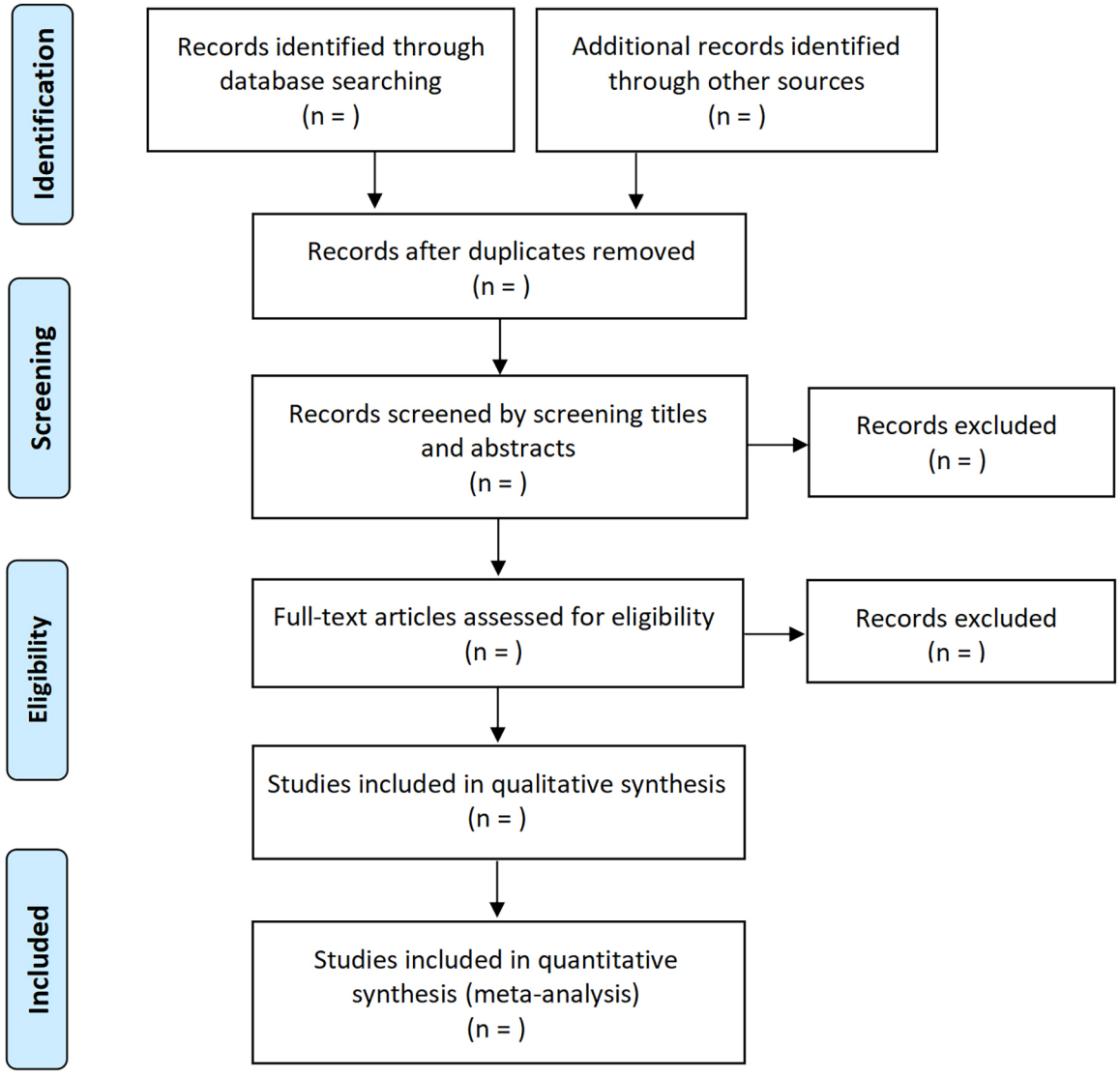

Figure 1 The flowchart for study selection.

results are robust and reliable. Another limitation is that the number of studies comparing the effects of different concentrations of ropivacaine for PNB may be relatively small, especially for subgroup analysis. Therefore, well-designed, large-sample RCTs may be needed to determine the optimal concentration of ropivacaine for PNB.

According to our protocol, subgroup analysis will recommend the optimal concentration of ropivacaine for a specific nerve block or general anaesthesia. Additionally, we will use the GRADE approach to assess the quality of evidence for primary outcomes. Therefore, this study may provide evidence to guide the clinical use of ropivacaine for PNB in adult patients.

Contributors Conceptualisation: YW and DZ. Methodology: JL and YW. Validation: JL, JP and YW. Writing original draft: JL, JP, YX, YiW and YW. Writing, review and editing: YW and DZ.

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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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