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Efficacy and safety of multimodal analgesia based on bolus versus continuous infusion of NSAIDs: a meta-analysis of randomized controlled trials

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ADMINISTRATIVE INFORMATION

Support - Nil.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202550045

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 16 May 2025 and was last updated on 16 May 2025.

INTRODUCTION

Review question / Objective The aim of this meta-analysis was to evaluate the efficacy and safety of continuous infusion versus bolus administration of NSAIDs after surgery.
(i) Population: adult patients.
(ii) Intervention: continuous infusion of NSAIDs (Nonsteroidal Anti-Inflammatory Drugs) (over 6 h) as a postoperative analgesia
(iii) Comparator: bolus administration of NSAIDs as a postoperative analgesia
(iv) Outcomes: Opioid consumption; incidence of PONV (postoperative nausea and vomiting), respiratory depression; need for rescue analgesia; pain score at 6, 12, 24, 48 h postoperatively.
(v) Study design: randomized controlled trials.

Rationale Multimodal analgesia is integral to enhanced recovery after surgery (ERAS) protocols, reducing opioid use and improving postoperative outcomes. Nonsteroidal anti-inflammatory drugs (NSAIDs) are central to multimodal analgesia, but the optimal method of NSAID administration—bolus versus continuous infusion—remains unclear. Bolus administration provides rapid drug delivery, while continuous infusion ensures more stable plasma concentrations over time. Theoretically, continuous infusion may offer more consistent analgesia, but its clinical advantage over bolus administration has not been conclusively established.

This meta-analysis aimed to compare the efficacy and safety of bolus versus continuous NSAID infusion in postoperative patients. The primary outcome was total opioid consumption, reflecting analgesic effectiveness, while secondary outcomes included pain intensity, postoperative nausea and vomiting, respiratory depression, and the need for rescue analgesia. By synthesizing data from randomized controlled trials (RCTs), the study provided evidence on the comparative effectiveness of both methods in reducing opioid use and improving pain management.

Condition being studied Continuous infusion of NSAIDs (Nonsteroidal Anti-Inflammatory Drugs)

with duration over 6 h or NSAIDs bolus injections as an analgesia regimen after elective non-cardiac surgery.

METHODS

Search strategy A systematic literature search of studies published until March, 2024 was conducted in PubMed (Medline) database by two independent investigators. Both backward and forward snowballing methods were also used for an exhaustive search (Litmaps service). Language restrictions were not applied.

Participant or population Adult patients (without restrictions on age, sex, race, or ethnicity).

Intervention Continuous infusion of NSAIDs with duration over 6 h as a postoperative analgesia regimen.

Comparator Bolus administration of NSAIDs as postoperative analgesia regimen.

Study designs to be included We included only randomized controlled trials.

Eligibility criteria We focused on randomized controlled trials that explored effectiveness and incidence of side effects of continuous versus bolus administration of NSAIDs. Studies were excluded if they met one of the following criteria: 1) were systematic reviews, letters to editors, etc.; 2) used a combination of analgesic drugs as a technique for investigation (incomparable groups); 3) there were no relevant outcome data.

Information sources PubMed (MThe primary outcome for this meta-analysis is total opioid consumption. edline) and databases from Litmaps service (Crossref, Semantic Scholar, OpenAlex).

Main outcome(s) The primary outcome for this meta-analysis was total opioid consumption.

Additional outcome(s) The secondary outcomes were incidence of PONV and respiratory depression, need for rescue analgesia, and pain score at 6, 12, 24, 48 h postoperatively.

Quality assessment / Risk of bias analysis The risk of bias of the included studies was assessed by three independent investigators using the RoB 2 tool. Publication bias and small-study effects were assessed using Egger's test and funnel plot analysis. The certainty of evidence were assessed with the GRADE systematic approach.

Strategy of data synthesis The following data were extracted by five independent researchers:
1. General information about the publication (first author, year of publication, journal, sample size);
2. Patient characteristics (mean age, mean weight, sex);
3. Information on surgical intervention, anesthesia, and the format of postoperative analgesia (type and duration of surgery, type of anesthesia, duration of postoperative analgesia, medications, and their administration route);
4. Outcome data: total opioid consumption during the observation period, proportion of patients reporting nausea and/or vomiting, proportion of patients experiencing respiratory depression episodes, and pain levels measured at 6, 12, 24, and 48 hours after the start of observation using the Visual Analogue Scale (VAS) or Numeric Rating Scale (NRS).
In the absence of pain scores for the specified time points, the following assumptions were made:
1. Measurements for the 4–8 hours postoperatively or the time point of 8 hours were used as pain score at 6 hours after surgery completion;
2. Measurements for 16 hours were used as pain level data for the 12-hour time point.
The data will be converted to the mean and 95% confidence interval format if needed.
STATA 18.0 (StataCorp LLC, Texas, USA) will be employed for both calculations and visualizations. The interstudy heterogeneity will be assessed via the I-squared (I^2) statistics and the Cochrane Q test. We are going to apply a random-effects model (restricted maximum likelihood [REML] method) for the meta-analysis. Statistical significance will be set at $p < 0.05$.

Subgroup analysis We performed subgroup analysis and meta-regression if applicable.

Sensitivity analysis We performed sensitivity analysis and meta-regression if applicable.

Language restriction No language limitations.

Country(ies) involved Russian Federation.

Keywords Analgesia; NSAIDs; Surgery; Parenteral Infusions; Drug Administration Routes.

Contributions of each author
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