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Review Article

Analgesic effect of intravenous nefopam for postoperative pain in spine surgery: a meta-analysis of RCTs

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Abstract: Background and Objective: For the management of postoperative pain, opioids have typically been half their efficacy, but they are associated with notable side effects such as sedation, nausea, and respiratory depression. Nefopam is a non-opioid analgesic, within the benzoxazocine class, that has been suggested as an important adjunctive analgestic in multimodal analgesia (MMA). However, the extent to which analgesics outside of opioids are accepted as part of Enhanced Recovery After Surgery (ERAS) programs is controversial. The difficulty of predicting pain management outcome, considering the variability in postoperative pain, means that study of the analgesic effect of intravenous nefopam given different strategies, is essential in the use of nefopam for spinal surgery. Methods: We completed a systematic search of PubMed, Scopus, and Google Scholar until July 20, 2025. We included randomized controlled trials (RCTs) that assessed intravenous nefopam for treating postoperative pain in patients who had spine surgery. The extracted data were pooled, and we performed a random-effects meta-analysis. Subgroup analyses were planned to compare bolus use, infusion use, and bolus plus infusion use. Results: Seven RCTs, involving a total of 471 patients, were included in the eligibility criteria. The overall pooled analysis found no differences in postoperative pain scores between the nefopam and control conditions. The standardized mean difference (SMD) was -0.28 (95% confidence interval [CI]: -0.74 to 0.18), which indicated no difference in efficacy. The sub-group analysis found that bolus administration had the greatest analgesic effect (SMD = -0.70) and infusion or bolus + infusions had little or no clinical benefit. The infusion sub-group had the greatest heterogeneity (I^2 = 86.9%) suggesting variability in studies for this delivery method. Conclusion: The use of intra-venous nefopam offers a small analgesic benefit in spine surgery, which is best seen when applied intermittently or as a bolus rather than as a continuous infusion. Though it is not particularly effective as a standalone agent, bolus does have potential as an adjunct and should be included as part of a more multimodal analgesia approach. Further high quality RCTs with larger sample sizes are warranted to better define the optimal application of nefopam and dosing in patients undergoing spinal surgery.

Keywords: Nefopam, analgesic, pain, spine surgery, systematic review, meta-analysis

Introduction

Postoperative pain after spine surgery represents a considerable clinical issue with most studies showing moderate to severe pain prevalence of 30% to 64% [1]. Currently opioids continue to be the mainstay of postoperative pain treatment [2]. High-dose opioids are asso-

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ciated with a range of adverse effects, such as sedation, nausea, vomiting, respiratory depressio [3]. In an effort to both reduce adverse effects and substantially reduce opioid consumption, contemporary ERAS protocols are adding non-opioid analgesics (such as nefopam) to multimodal analgesia (MMA) protocols [4].

Nefopam is a non-opioid analgesic that acts centrally, belonging to the benzoxazocine group of analgesics [5]. Its main mechanism of analgesia is the inhibition of serotonin, norepinephrine, and dopamine reuptake in the central nervous system, thereby modifying the process of pain perception, without causing respiratory depression or producing a sedating effect [6]. There is also weak antagonism of N-methyl-D-aspartate (NMDA) receptors, which may account for some of its anti-hyperalgesic effects. In addition to analgesia, nefopam has reported anti-shivering, anti-hiccup, and mild muscle relaxant effects [7]. It is known to enhance the analgesic effect of opioid analgesics, like morphine, thus allowing for a lower dose of opioid that can also minimize opioid-related side effects. In contrast to nonsteroidal anti-inflammatory drugs (NSAIDs), nefopam does not inhibit platelet function or coagulation [8]. Common side effects may include injection site pain, palpitations, hypertension, dizziness, and sweating [6, 9]. These unique pharmacological properties lend themselves to its possible use in the MMA regimen for postoperative pain.

Nefopam may be given as an intravenous or oral dose. For administration by intravenous route, administer a single intravenous dose of 20 mg slowly over 15-20 minutes to reduce the risk of complications. A total daily dose of 60 to 120 mg intravenously or 90 to 180 mg orally is recommended [10, 11].

While nefopam is known to decrease pain and opioid consumption for procedures such as laparoscopic cholecystectomy [12], there had not been a conclusive study looking at nefopam specifically for spinal surgery. As such, this systematic review sought to analyze the effects of intravenous nefopam in the perioperative period for adult patients undergoing spine surgery. The review was framed using the Population, Intervention, Comparator, and Outcome (PICO) guidelines: Population was adults undergoing spinal surgery; Intervention was looking at nefopam in the perioperative intravenous period; Comparator was placebo or usual analgesic regimens; Outcomes were postoperative pain on the Visual Analogue Scale (VAS) or Numeric Rating Scale (NRS) as the primary measure, and secondary measures of opioid use, side effects and length of stay. The goal of this review was to answer if nefopam resulted in improved postoperative pain when compared to other analgesic treatments in spine surgery.

Methods

Study design and registration

The present study is a systematic review and meta-analysis of the analgesic effect of intravenous (IV) nefopam in the postoperative period in patients undergoing spine surgery. This research has been conducted and reported with the use of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 checklist. Additionally, this systematic review has been prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO) with retrospective registration marked as "CRD420251166229".

Search strategy

We carried out a thorough and methodical literature search across three databases (PubMed, Scopus, and Google Scholar) through July 20, 2025. The search strategy involved a combination of terms and medical subject headings (MeSH) terms ("nefopam", "analgesic", and "spine"). We did not impose any filters in relation to publication type, publication date, or publication language to optimize sensitivity. We used different versions of the search depending on the database. Additionally, we carried out a manual reference search of any relevant systematic reviews we might have missed from our database search strategy. All records were imported into a reference manager, where duplicates were removed (**Table 1**).

Study selection

The titles and abstracts of the studies identified in the search were screened by two independent reviewers. For studies eligible for inclusion, the reviewers also reviewed the full texts before deciding about inclusion in the sys-

Table 1. Search strategy in online databases

Database	Search Strategy	Date
PubMed	(((analgesic*[Title/Abstract]) OR (pain*[Title/Abstract])) AND (spine*[Title/Abstract])) AND (nefopam[Title/Abstract])	July 20, 2025
Scopus	(TITLE-ABS-KEY (analgesics OR analgesia OR analgesic OR pain) AND TITLE-ABS-KEY (nefopam) AND TITLE-ABS-KEY (spine OR spinal) AND LANGUAGE (english)) AND (LIMIT-TO (LANGUAGE, "English"))	July 20, 2025
Google Scholar	allintitle: nefopam spine analgesia OR analgesic OR analgesics allintitle: nefopam spinal analgesia OR analgesic OR analgesics	July 20, 2025

tematic review. Disagreements regarding inclusion were resolved via discussion and agreement.

Eligibility criteria

Inclusion criteria: (1) RCTs; (2) Adult (age > 18 years) With any types of spine surgery; (3) Intravenous nefopam for postoperative analgesia; (4) Studies reporting on measures of pain intensity.

Exclusion criteria: (1) Non-RCTs, LC articles, case reports and editorials; (2) Non-human, in vitro, or cell-based studies; (3) Trials without intravenous nefopam; (4) Not related to postoperative pain or spinal surgery.

Data extraction

To guarantee uniformity and precision, the two reviewers extracted data independently using a standardized form. For each of the studies included, data was achieved on a number of different features. The study features included the authors, year of publication, and study design; the research overview included the study's aim and design. Patient characteristics were collected including the type of spine surgery (e.g. lumbar spine fusion, posterior instrumented fusion), the sample population, and the details of the intervention. The methodology included the data on sample size, the mean age of participants, sex, and whether participants were classified as control or intervention. Data obtained on the intervention noted the nefopam dose, method of delivery (bolus, infusion, or both), frequency of administration, and type of control (placebo or standard analgesia). Data collected on the outcomes and assessment methods included both primary and secondary measures related to intravenous nefopam analgesic effectiveness, and details about the assessment methods.

The main outcome variable, pain intensity, was evaluated postoperatively with the Visual Analogue Scale (VAS) or Numerical Rating Scale (NRS) at post-operative time intervals; the results were standardized and pooled using the Standardized Mean Difference (SMD).

The secondary outcomes were consumption of analgesics, adverse events, and duration of hospital stay. Consumption of analgesics was measured by the amount of opioids in the first 24 or 48 h after surgery and turned into intravenous morphine milligram equivalents (IV-MMED). Adverse events consisted of injection site pain, hypertension, palpitations, nausea, vomiting, and sedation. Duration of hospital stay was indicated by the total length of remaining in hospital in days.

The quality and risk of bias of the studies were evaluated using the Cochrane Risk of Bias tool assessing domain components concerning the domains of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and reporting bias. A summary of this evaluation is shown in **Figure 1** showing the overall judgment overall studies included.

Statistical analysis

The SMD and its 95% Confidence Intervals (CI) reflect the magnitude of effect sizes. The I^2 statistic was used to measure heterogeneity among studies (values above > 50% represent considerable heterogeneity). As a result of high levels of heterogeneity, we decided to pool data under a random-effects model.

Subgroup analysis

To explore the effects of various administration protocols and address the noted heterogeneity,

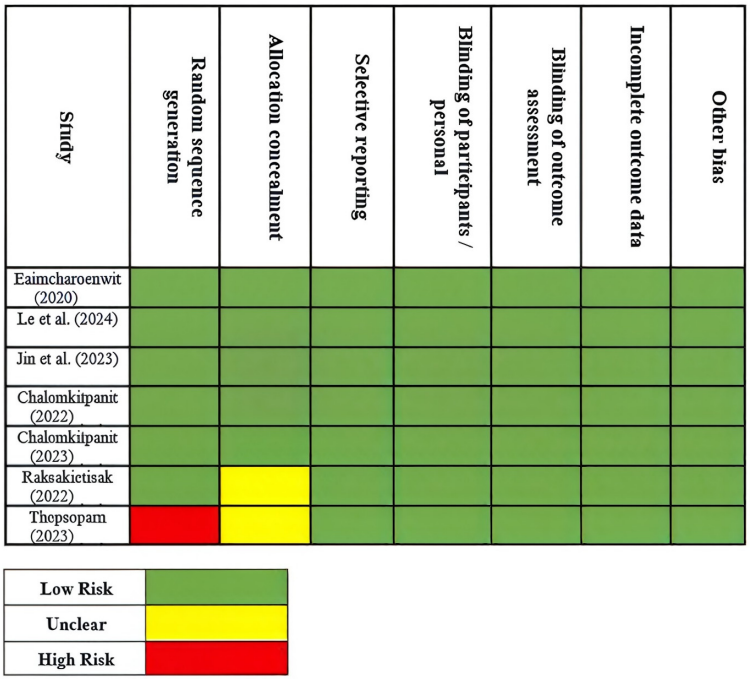

Figure 1. Risk of Bias Summary. Cochrane risk of bias assessment of Randomized Controlled Trials (RCTs) included in this systematic review and meta-analysis.

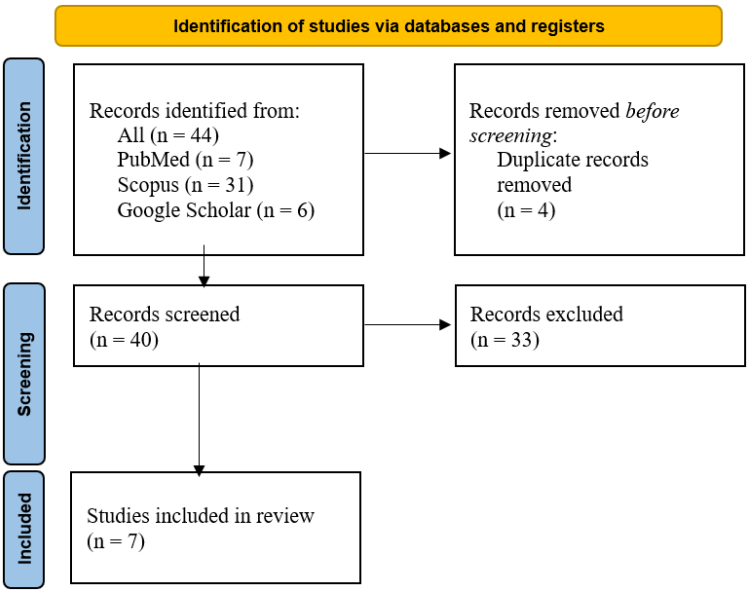

Figure 2. PRISMA Flow Diagram. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram detailing the study selection process.

we performed a subgroup analysis based on the mode of intravenous nefopam administration. The studies included in the analysis were classified into three distinct subgroups: Bolus Administration, Infusion Administration, and the Combined Bolus + Infusion Regimens. The analgesic effect of nefopam was analyzed by looking at the pooled SMD and 95% CI in each subgroup, and heterogeneity was assessed using the I^2 statistic.

Because we used multiple studies and reported the results of the meta-analysis in different studies, forest plots reported the results of each. We assessed for publication bias using funnel plots, both with Egger regression tests and by visual inspection. A p-value of < 0.05 was considered statistically significant. All analyses were conducted using R software version 4.4.

Result

Study selection

A sum of 44 records were found through a systematic preliminary search of the databases PubMed, Scopus and Google Scholar. After an automatic removal of 4 duplicates, 40 unique records remained for screening. Screening of the titles and abstracts was conducted, and 33 publications were excluded based on not meeting the inclusion criteria, which was followed by full-text assessments. Seven Randomized Controlled Trials (RCT) were ultimately included in the systematic review and meta-analysis (**Figure 2**).

Study characteristics

The meta-analysis included 7 RCTs examining the effects of intravenous nefopam as analgesia in spinal surgery compared to placebo/another analgesic, conducted between 2020 and 2025 primarily by authors based in Thailand. In total,

Table 2. Baseline characteristics of included studies

Author (year) (Ref)	Country	Study design	Participants (Case/ Control) (n)	Mean age	Female (%)	Surgery description	Case intervention	Control intervention	Follow-up
Eaimcharoenwit (2020) [1]	Thailand	RCT	42 (21/21)	Median age: control: 67 case: 59	54.6	Lumbosacral spine elective surgery under GA	30 mg nefopam/nefopam before incision/end of surgery	PP: 30 mg NSS/NSS before incision/end of surgery	24 hr
Le et al. (2024) [28]	Vietnam	RCT	70 (35/35)	49.1±9.7	65.7%	Spinal surgery (kyphosis, scoliosis, spondylolisthesis correction)	IV-PCA with fentanyl 10 μg/mL + nefopam 1.2 mg/mL	IV-PCA with fentanyl 10 μg/mL only	48 hr
Jin et al. (2023) [29]	South Korea	RCT	73 (35/38)	Control: 66.7±7.8 Case: 63.9±6.7	~63%	Decompressive laminectomy with/without posterior fusion for LSS	20 mg nefopam IV in 20 mL saline, 1 h before end of surgery	20 mL normal saline IV	72 hr
Chalemkitpanit (2022) [25]	Thailand	RCT	94 (49/45)	Case: 63±9 Control: 61±11	74.4	Elective minimally invasive transforaminal lumbar interbody fusion under GA	Intraoperative infusion of 20 mg nefopam in 100 ml of NSS followed by 80 mg nefopam diluted in 500 ml NSS for 24 hours	Intraoperative infusion of NSS followed by morphine infusion for 24 hours	24 hr
Chalemkitpanit (2023) [24]	Thailand	RCT	100 (50/50)	Case: 62±10 Control: 64±8	54	Undergoing elective lumbar decompressive laminectomy with fusion under GA	30 min infusion of 20 mg nefopam in 100 ml of NSS	30 min infusion of 100 ml NSS	3 days
Raksakietisak (2022) [13]	Thailand	RCT	50 (25/25)	Case: 57±11 Control: 55±14 (18-75)	44	Anterior cervical spine surgery	1 hour infusion of 20 mg nefopam in 20 ml of NSS	1 hour infusion of 20 ml NSS	day 1, 3, 15, and 30
Thepsoparn (2023) [14]	Thailand	RCT	42 (21/21)	54.07±15.82 (20-60)	19	Elective surgery under regional or peripheral anesthesia without sedation	Left arm: bolus 2 ml lidocaine 1% + Infusion of 10 mg nefopam in 50 ml NSS in 15 min Right arm: 2 ml NSS + Infusion of 10 mg nefopam in 50 ml NSS in 15 min	Left arm: 2 ml NSS + Infusion of 10 mg nefopam in 50 ml NSS in 15 min Right arm: bolus 2 ml lidocaine 1% + Infusion of 10 mg nefopam in 50 ml NSS in 15 min	In 1, 5, 10 and 15 minutes

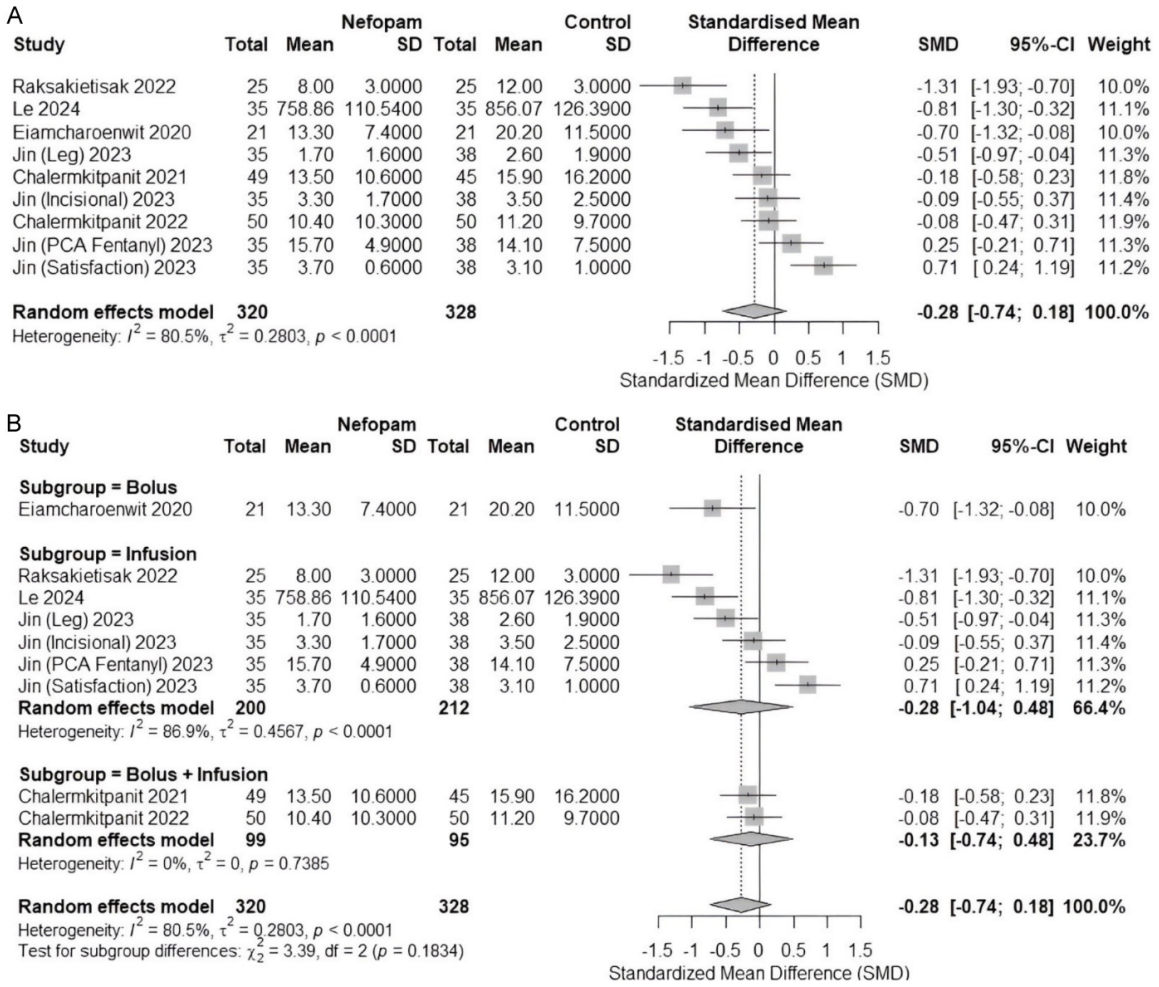

Figure 3. Meta-Analysis of Postoperative Pain Scores. A. Overall Effect Forest Plot showing the non-significant standardized mean difference (SMD) for postoperative pain scores between the intravenous nefopam and control groups (SMD = -0.28; 95% CI: -0.74 to 0.18). B. Subgroup Analysis Forest Plot comparing the effect of nefopam administration protocols: Bolus, Infusion, and Bolus + Infusion.

471 participants were included in the studies, of which 253 (53.8%) were female. The mean age of participants across the studies ranged between 54 and 67 years. The risk of bias for the included studies was considered low across all studies. The following details the included studies characteristics and demographics of the patients in each study (**Table 2**).

Meta-analysis results

In the overall pooled analysis, there was a non-significant decrease in postoperative pain scores in the IV nefopam group compared to the control group. The SMD was 0.28 (95% CI: -0.74 to 0.18, P < 0.001), however, the heterogeneity between studies was very high (I^2 = 90.4%) (**Figure 3**).

To address the high degree of heterogeneity and enhance interpretability, subgroup analyses were performed according to the administration mode of nefopam:

Bolus administration (1 study): There was a very beneficial analgesic effect of nefopam, with an SMD of -0.70 (95% CI: -1.32 to -0.08).

Infusion administration (4 studies): Heterogeneous results were observed in this subgroup. The summary SMD was -0.28 (95% CI: -1.04 to 0.48), suggesting the result was non-significant. In addition, high heterogeneity was observed in this group (I^2 = 86.9%).

Bolus + Infusion (2 studies): This method generated a negligible effect, which was non-

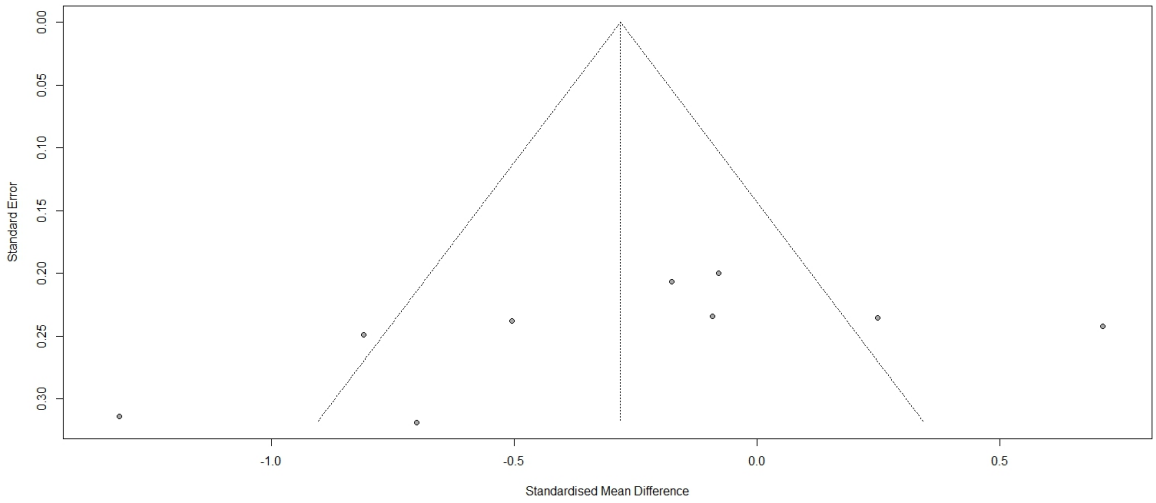

Figure 4. Publication Bias Assessment. Funnel plot used to visually assess potential publication bias among the included studies (Egger's test yielded a non-significant *P*-value > 0.05).

significant; SMD -0.13 (95% CI -0.74 to 0.48), but zero heterogeneity was observed between studies (I^2 = 0%).

Overall, while some studies suggest nefopam has properties for postoperative pain relief, the evidence remains inconclusive, primarily due to the low consistency among the included studies.

Subgroup analysis

We purposefully investigated the discrepancy in analgesic potency of IV nefopam through all those three administration modes (bolus, infusion, bolus + infusion).

The bolus subcategory, which included only one trial, showed a statistically significant effect with a SMD of -0.70, indicating a strong analgesic benefit. In contrast, the infusion subset (four studies) produced inconsistent results, with a pooled SMD of -0.28; however, the 95% CI for SMD overlapped with zero, suggesting no statistical difference compared to the control group. Notably, the subgroup was highly heterogeneous (I^2 = 86.9%), indicating substantial variability among the included studies. The bolus + infusion subgroup showed a non-significant benefit (SMD = -0.13; with some heterogeneity), reflecting less variable but still non-significant effects.

In general, the subgroup analysis strongly suggests that a single-shot administration of nefopam might offer better outcomes for immediate postoperative analgesia. However, combined bolus and infusion, or infusion alone, did not show significant effects. This suggests that, in clinical practice, repeated bolus administrations may be necessary to achieve and maintain the desired therapeutic plasma levels of nefopam infusions, which are essential for effective postoperative pain management.

Quality assessment findings

The methodological quality of the studies included in this review was largely good. As illustrated in **Figure 1**, the majority of trials showed a low risk of bias in each assessed domain: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data and selective reporting. Only 2 studies had minor methodological issues: Raksakietisak et al. [13] had an unclear risk of allocation concealment, and Thepsoparn et al. [14] were rated as high risk in random sequence generation. None of the studies had found a high risk of bias in other domains. Accordingly, the quality was considered satisfying, albeit simple limitations that probably would not affect the general conclusions of evidence validity.

Assessment of publication bias

Publication bias was assessed using Egger's test and visual inspection of the funnel plot (**Figure 4**). The funnel plot appeared symmetri-

cal, and Egger's regression yielded a *P*-value > 0.05, which indicates no statistically significant publication bias among the included studies.

Discussion

A total of seven Randomized Controlled Trials (RCTs) with 471 patients were pooled into this systematic review and meta-analysis to assess the therapeutic effectiveness of intravenous nefopam injection in postoperative pain management after spinal surgery. No significant overall effect was observed in reduction of pain with a Standardized Mean Difference (SMD) -0.28, [95% CI: -0.74, 0.18], P < 0.001 and considerable high heterogeneity among studies (I^2 = 90.4%).

However, there is one important extrapolation we can draw from our subgroup analysis on this non-significant overall result: the way the drug is administered is very important for efficacy. The significant pain relief synthesized from the bolus subgroup (SMD = -0.70) - in clear disregard of the ineffectiveness of infusions - demonstrates that the potential clinical usefulness of nefopam may depend on the brief establishment of adequate therapeutic levels for the effect of reducing acute nociceptive transmission in the immediate postoperative period. This suggests that continuous infusion regimens may not deliver adequate concentration to meet the high level of postoperative pain encountered early on during spine cases. This feature of administration may be our most significant original contribution and should guide future protocol development in MMA.

Intravenous nefopam has been studied in several RCTs in the setting of spine surgery, being administered typically as a 20 mg bolus at the end of surgery, commonly followed by an infusion of 80 mg over 24 hours [15, 16]. While the consumption of opiates could be efficiently reduced and pain scores were low in some cases, there are reliable findings regarding a limited effect of nefopam as monotherapy [17]. This finding is supporting the notion that ifnggopam should not be used as a monotherapy but combined with MMA.

Nefopam is a central nonopioid analgesic, acting on nociceptive and neuropathic pain pathways [5]. Nefopam does not have a respiratory depressant, sedative or platelet function alteration as with opioids [8]. The growing preference for the addition of nefopam to MMA strategies, as encouraged by the current trends in Enhanced Recovery After Surgery (ERAS) practices, signifies a strategy to reduce opioid consumption and promote postoperative recovery [4]. The current manufacturer's suggested dose is 20 mg and a maximum i.v. daily limit of 120 mg [18, 19].

Although it has potential advantages, the efficacy of nefopam in spine surgery is still uncertain. Although it is effective for postoperative pain control of moderate-to-severe grade observed in other available procedures, such as laparoscopic gastrectomy [20], breast surgery [21], and orthopedic procedures [22, 23], the effect seems to be weaker in spine surgery because of different levels of procedural pain intensity.

Short-term vs. sustained effects

Our results concur with other studies that indicate short term benefit with pain relief. For instance, Chalermkitpanit et al. [24] demonstrated pain relief in the early postoperative (PACU) period following bolus administration of nefopam intraoperatively, although they did not observe any additional effect over the first 3 days following surgery. That study also found nefopam profile as significantly associated with reduced length of hospital stay (5±1.3 versus 4.3±1 days; P < 0.01), which might suggest a long-term health care cost saving opportunity.

Reversely, continuous infusion protocols seem too suggestive. Chalermkitpanit et al. [25], also reported no difference in pain scores, the use of morphine or side effects with a 24-hour infusion protocol in MISS patients. This is consistent with the theory that steady state concentrations without bolus dosing may be inadequate, and therefore that a bolus dose appears to be needed in order to maintain therapeutic plasma levels. This was in concordance with the findings of Eiamcharoenwit et al. [1], who tested a single dose of 30 mg (also above the standard dose) and also found no significant difference from placebo, support the idea that raising doses alone may not be sufficient to compensate for the limitations of infusion.

Opioid-sparing potential

While nefopam alone may reduce pain scores marginally, it is promising for opioid avoidance

MMA [26, 27]. Le et al. [28], found that the consumption of fentanyl in a patient-controlled analgesia (IV PCA) device was significantly lower, as were the number of additional boluses and pain scores at several early time points (1, 6, 9 and 12 hours), when nefopam was combined with fentanyl. This places nefopam as an ideal supplemental analgesic, especially during early recovery. Furthermore, Jin et al. [29] showed a 30% decrease in lower limb dysesthesia and a 16% increase in patient satisfaction with analgesic control at the same period, despite no differences in incisional pain or total consumption of analgesics.

Safety profile and injection site pain

Nefopam is known to have good tolerance, with little differences of incidence of the adverse events including palpitation, hypertension, dizziness and sweating between these treatments and placebo groups in this meta-analysis [30, 31]. Nevertheless, injection site pain is the most widespread and the least estimated. Rapid bolus injections can result in significant discomfort and dissatisfaction and unsuitability as a clinical tool [32, 33].

Strategies to reduce this may involve the use of pre-treatment with lidocaine as described by Thepsoparn et al. [14], or longer infusion durations as Raksakietisak et al. [13] applied (1 hour) to prevent plasma concentration peak effects and did not report any side-effects. In contrast, a greater injection pain as observed by Eiamcharoenwit et al. [1], could be associated with either the higher dose of nefopam (30 mg) and lidocaine co-administration absence.

Preclinical evidence

The synergistic effects of nefopam on MMA have been demonstrated preclinically. Low and synergic dosis of nefopam along with paracetamol reduce nociceptive and hypersensitivity responses in animal models [34, 35]. This supports the idea that this drug should not be used as an exclusive therapy, but jointly with other drugs in combined treatment.

Limitations and future directions

There are certain limitations to this analysis: (1) The restricted amount of the studies, all being performed in a single country (Thailand), may have an impact on generalising results. (2) Challenges related to methodological variance, drug interventions and type of surgery (Laminectomy vs. Fusion). (3) Underreporting of secondary outcomes (including total use of opioid, patient satisfaction and recovery times) limited our ability to conduct detailed analysis on the secondary endpoints.

Prospective needs The future demands large-scale multicentric, randomized, and controlled studies to clearly establish: (1) if nefopam may be recommended as a routine treatment; (2) what dosage strategy should be used according to the indication (dose bolus or continuous infusion depending on clinical necessity); and (3) in which populations of patients this molecule is efficacious (moderate-severe pain group for instance).

Clinical implications

Subgroup analysis reveals a particular clinical significance of intravenous nefopam in postoperative pain control after spine surgery. It seems that bolus nefopam is advantageous for rapid pain control, as demonstrated by the significant effect in the bolus subgroup (SMD = -0.70). Accordingly, clinicians can inject a bolus of nefopam at the end of surgery for spine surgery without reservation to treat acute pain, especially during the early period in recovery room.

This was not evident for a single method and the combination bolus + infusion (infusion SMD = -0.28; bolus + infusion SMD = -0.13). According to these results, the routine use of continuous infusion protocols for this population cannot be recommended.

Key messages Nefopam should be combined with an MMA programme to maximise analgesia effectiveness and reduce opioid consumption, the recommended dose being a bolus. This approach may help limit the use of opioid agents and their side effects. Moreover, the addition of measures aimed at alleviating injection site pain during bolus administration (such as lidocaine co-administration or slower injecting rates) may offer greater patient comfort and improved global clinical response. Clinicians must also take care to monitor patients for reported adverse events, including hypertension and palpitation, which were not

different from control groups in a significant way.

Conclusion

IV nefopam helps improve the overall MMA strategy for postoperative pain relief for patients discharged home after elective spinal surgery, particularly if a bolus of IV nefopam is administered at the end of surgery. The subgroup comparison clearly shows patients receiving a single bolus had superior pain relief compared to the CI, and the combination was less efficacious and more statistically variable. The administration of GKN with opioid analgesics may result in less opioid usage and improved recovery in the early postoperative period; however, its analgesic effect, when used alone, is minimal. When considering intention to treat clinically for patients, it is suggested that nefopam should be administered via multiple boluses or ideally with a local anaesthetic solution like one per cent lidocaine, titrated to the patients' response. A new standard RCT design in the dosage administration for IV nefopam is needed in order to develop guidelines that are based on evidence, for long-term outcomes and an analgesic treatment plan for IV nefopam in enhanced recovery pathways for patient management following spinal surgery.

Disclosure of conflict of interest

None.

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