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(Abstract)

Contents

The Efficacy of Perioperative Pharmacological and Regional Pain Interventions in Adult Spine Surgery: A Network Meta-Analysis and Systematic Review of Randomized Controlled Trials

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Introduction: The development of a widely accepted standardized analgesic pathway for adult spine surgery was hampered by difficult interpretation of the current literature in pain management [1, 2]. We conducted a systematic review and network meta-analysis to compare and rank different pharmacological and regional interventions used in adult spine surgery.

Methods: Ethics approval was not applicable because the study did not involve human or animal research. A predefined protocol was published at PROSPERO (CRD42020171326). A systematic search was performed in MEDLINE, Embase, and a variety of other sources from their inception to January 25, 2021. Study screening, selection, and data extraction were performed by two independent investigators. We included all randomized controlled trials investigating either pharmacological or regional interventions for acute postoperative pain management in adults undergoing spine surgery. The co-primary outcomes were cumulative opioid consumption (in intravenous morphine equivalents) and visual analogue score (VAS) of pain (range 0-10) at postoperative 24 hours. A network meta-analysis was performed using the Bayesian approach (random-effect model) to synthesize the direct and indirect effects of all interventions. We also performed a meta-regression to assess the effects of the use of pharmacological agents in the postoperative period against the use in preoperative or intraoperative period.
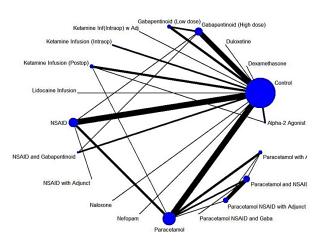
Results: We screened 4054 studies and included 88 studies comprised of 6621 participants. Nine out of 19 pharmacological intervention combinations were effective at reducing both opioid consumption and pain score against placebo (Fig 1). The most effective interventions were triple-agent therapy, consisting of paracetamol and NSAID with adjunct (MD (morphine) -26 [95% Credible Interval (CrI): -39 to -12] mg and MD (VAS) -2.2 [95% CrI -3.0 to -1.4]), or paracetamol, NSAID, and gabapentinoid (MD (morphine) -28 [95% CrI: -53 to –3] mg and MD (VAS) -1.5 [95% CrI: -2.4 to -0.7]). Double-agent therapy, high-dose gabapentinoid (gabapentin ≥ 900 mg/day or pregabalin ≥ 300 mg/day) and ketamine infusion were less effective, with morphine reduction of 15-18 mg and pain score reduction of 1-1.5. Single-agent interventions were largely ineffective. No regional intervention was found to reduce both co-primary outcomes, with the caveat that all regional interventions studied for opioid consumption were only given as single-shot injections. Our meta-regression showed all but one pharmacological interventions were only effective when they were used in the postoperative period. The risk of bias was overall low amongst all studies. There was no inconsistency nor publication bias.

Conclusion: Triple-agent multimodal therapy consisting of paracetamol and NSAID with either adjunct or gabapentinoid is the most effective pain intervention in adult spine surgery. A graded treatment response is found supporting multimodal pain management against double- or single-agent management. Pharmacological agents given as single dose in preoperative or intraoperative period are not effective at reducing pain score and opioid consumption.

REFERENCES:

1. Alboog A, Bae S, Chui J (2019) Anesthetic management of complex spine surgery in adult patients: a review based on outcome evidence. Curr Opin Anaesthesiol 32:600–608.
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A

Gabapentinoid (Low dose)
Gabapentinoid (High dose)
Ketamine Inf(Intraop) w Adj
Ketamine Infusion (Intraop)
Duloxetine
Ketamine Infusion (Postop)
Dexamethasone
Lidocaine Infusion
Control
NSAID
Alpha-2 Agonist
NSAID and Gabapentinoid
Paracetamol with /
NSAID with Adjunct
Paracetamol and NSAII
Naloxone
Paracetamol NSAID with Adjunct
Nefopam
Paracetamol NSAID and Gaba
Paracetamol

B

Gabapentinoid (High dose)
Gabapentinoid (Low dose)
Duloxetine
Ketamine Inf(Intraop) w Adj
Dexamethasone
Ketamine Infusion (Intraop)
Control
Ketamine Infusion (Postop)
Buprenorphine Patch
Lidocaine Infusion
Alpha-2 Agonist
NSAID
Paracetamol with Adjunct
NSAID and Gabapentinoid
Paracetamol and NSAID
Naloxone
Paracetamol NSAID with Adjunct
Nefopam
Paracetamol NSAID and Gaba
Paracetamol

C

Intervention		MD (95% CI)	
NSAID with Adjunct		-29.26 (-47.50 to -11.16)	*
Paracetamol NSAID with Adjunct		-25.66 (-38.93 to -11.90)	*
Paracetamol NSAID and Gaba		-28.22 (-52.85 to -2.97)	*
Gabapentinoid (High dose)		-18.10 (-24.59 to -11.72)	*
Paracetamol and NSAID		-16.74 (-29.01 to -4.24)	*
Paracetamol with Adjunct		-16.14 (-28.10 to -4.06)	*
Ketamine Infusion (Postop)		-15.49 (-25.44 to -5.85)	*
NSAID and Gabapentinoid		-14.58 (-26.16 to -3.11)	*
NSAID		-14.31 (-20.31 to -8.48)	*
Alpha-2 Agonist		-9.45 (-21.32 to 2.48)	
Lidocaine Infusion		-8.91 (-27.71 to 10.32)	
Ketamine Infusion (Intraop)		-9.21 (-21.49 to 3.16)	
Nefopam		-8.53 (-26.84 to 9.35)	
Naloxone		-7.82 (-25.04 to 9.31)	
Dexamethasone		-6.82 (-23.88 to 10.50)	
Gabapentinoid (Low dose)		-7.47 (-17.09 to 2.04)	
Ketamine Inf(Intraop) w Adj		-6.17 (-24.78 to 12.54)	
Paracetamol		-7.35 (-13.31 to -1.41)	*
Duloxetine		-2.08 (-19.03 to 15.11)	

D

Intervention		MD (95% CI)	
Paracetamol NSAID with Adjunct		-2.22 (-3.04 to -1.39)	*
Ketamine Infusion (Postop)		-1.78 (-2.34 to -1.21)	*
Paracetamol with Adjunct		-1.54 (-2.32 to -0.77)	*
Paracetamol NSAID and Gaba		-1.52 (-2.35 to -0.70)	*
Paracetamol and NSAID		-1.33 (-2.12 to -0.56)	*
NSAID		-1.12 (-1.48 to -0.78)	*
Paracetamol		-1.06 (-1.48 to -0.64)	*
Buprenorphine Patch		-1.06 (-2.15 to 0.00)	
Lidocaine Infusion		-0.95 (-1.87 to -0.04)	*
NSAID and Gabapentinoid		-0.84 (-1.49 to -0.20)	*
Gabapentinoid (High dose)		-0.83 (-1.22 to -0.45)	*
Ketamine Inf (Intraop) w Adj		-0.68 (-1.42 to 0.06)	
Alpha-2 Agonist		-0.55 (-1.32 to 0.22)	
Dexamethasone		-0.49 (-1.77 to 0.81)	
Ketamine Infusion (Intraop)		0.43 (-2.84 to 3.84)	
Gabapentinoid (Low dose)		-0.23 (-0.84 to 0.39)	
Naloxone		-0.15 (-1.18 to 0.90)	
Duloxetine		-0.00 (-1.11 to 1.12)	
Nefopam		0.18 (-1.09 to 1.44)	

Figure 1: Network meta-analysis of eligible comparisons of pharmacological interventions at postoperative 24 hours for (A) total opioid consumption and (B) pain score. Forest plots of network meta-analysis of all trials of pharmacological interventions at postoperative 24 hours for (C) total opioid consumption and (D) pain score