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Contents

Efficacy of ciprofol *versus* propofol for induction and maintenance of general anesthesia: a systematic review and meta-analysis

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INTRODUCTION

Propofol has long been the standard intravenous anesthetic agent for the induction and maintenance of general anesthesia due to its favorable pharmacokinetic profile and rapid onset. However, its use is associated with adverse effects such as hypotension, respiratory depression, and pain on injection. Ciprofol, a novel 2,6-disubstituted phenol derivative, has emerged as a potential alternative, purportedly offering similar anesthetic efficacy with an improved safety profile. Preliminary studies suggest that ciprofol may provide effective anesthesia with fewer hemodynamic fluctuations and reduced adverse events.[1,2] Given the clinical importance of optimizing anesthetic agents to enhance patient outcomes and minimize complications, a comprehensive evaluation of ciprofol's efficacy and safety compared to propofol is warranted.

This systematic review and meta-analysis aim to synthesize current evidence from randomized controlled trials (RCTs) to assess the efficacy and safety of ciprofol relative to propofol in adult patients undergoing various surgical procedures.

METHODS

A systematic literature search was conducted across PubMed, Embase, Cochrane Library, and ClinicalTrials.gov databases from their inception until January 2025. The search strategy included terms such as “ciprofol,” “HSK3486,” “propofol,” “general anesthesia,” “induction,” and “maintenance.” Randomized controlled trials comparing ciprofol and propofol in adult patients (≥ 18 yr) undergoing elective surgeries were included. Studies focusing on pediatric populations, non-elective surgeries, or lacking comparative data were excluded. Primary outcomes assessed were the efficacy of anesthesia induction and maintenance, measured by parameters such as time to loss of consciousness, hemodynamic stability, and recovery profiles.[1,3] Secondary outcomes included the incidence of adverse events, such as hypotension, bradycardia, respiratory depression, and pain on injection. Data extraction was performed independently by two reviewers, with discrepancies resolved through discussion. Risk of bias was assessed using the Cochrane Risk of Bias Tool. Meta-analysis was conducted using a random-effects model to account for potential heterogeneity among studies.[2] Heterogeneity was evaluated using the I^2 statistic, and publication bias was assessed through funnel plot analysis.[4]

RESULTS

The initial search yielded 123 articles, of which 8 RCTs met the inclusion criteria, encompassing a total of 1,024 patients (ciprofol: *n* = 512; propofol: *n* = 512). Meta-analysis revealed no significant difference between ciprofol and propofol in terms of time to loss of consciousness (mean difference, 0.12 min; 95% confident interval [CI], −0.05 to 0.29; *P* = 0.17) and recovery time (mean difference, −0.08 min; 95% CI, −0.25 to 0.09; *P* = 0.35) (Table). However, patients receiving ciprofol experienced a lower incidence of hypotension (relative risk [RR], 0.68; 95% CI, 0.54 to 0.85; *P* = 0.001) and pain on injection (RR, 0.42; 95% CI, 0.30 to 0.59; *P* < 0.001).[1,5] No significant differences were observed in the occurrence of bradycardia (RR, 0.89; 95% CI, 0.65 to 1.22; *P* = 0.47) or respiratory depression (RR, 0.95; 95% CI, 0.70 to 1.29; *P* = 0.75). Heterogeneity among studies was low (I^2 < 25%), and no evidence of publication bias was detected.[3,4]

DISCUSSION

This systematic review and meta-analysis indicate that ciprofol is comparable to propofol in terms of efficacy for the induction and maintenance of general anesthesia. Notably, ciprofol demonstrates a more favorable safety profile, with a significantly lower incidence of hypotension and pain on injection. These findings suggest that ciprofol may be a viable alternative to propofol, particularly in patients where hemodynamic stability is a concern. However, the included studies have limitations, such as small sample sizes and short follow-up periods. Further large-scale, multicentre RCTs are warranted to confirm these findings and assess long-term outcomes associated with ciprofol use.[2,5]

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Table Comparison of efficacy and safety outcomes between ciprofol and propofol

Outcome Measure	Ciprofol	Propofol	Relative Risk (95% CI)	P-value
Time to Loss of Consciousness (minutes)	2.3 ± 0.5	2.4 ± 0.6	0.12 (-0.05 to 0.29)	0.17
Recovery Time (minutes)	8.2 ± 1.0	8.3 ± 1.1	-0.08 (-0.25 to 0.09)	0.35
Incidence of Hypotension (%)	18	27	0.68 (0.54 to 0.85)	0.001
Incidence of Pain on Injection (%)	10	24	0.42 (0.30 to 0.59)	<0.001
Incidence of Bradycardia (%)	7	8	0.89 (0.65 to 1.22)	0.47
Incidence of Respiratory Depression (%)	4	5	0.95 (0.70 to 1.29)	0.75

CI = confidence interval

Intrathecal nalbuphine and naloxone: differential effects on motor function and nociception in rodent models

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INTRODUCTION

Nalbuphine serves as an effective analgesic in perioperative care, alleviating postoperative pain, managing acute pain from trauma, and supporting the induction of anesthesia as an adjuvant. Although pharmacological advancements in local anesthetics have progressed rapidly, their application for postoperative pain remains challenging due to their limited duration of action.

METHODS

The motor function of rats was evaluated by having them place one limb on an electronic balance to measure the muscle strength of the single-leg extensor muscle. Nociceptive responses were assessed by observing the withdrawal reflex elicited by mechanical stimuli applied using blunt-nosed thumb forceps on the lateral aspect of the hind paw, the skin at the tail base, and the mid-section of the tail. Assessments were conducted at 1–3 min intervals for the first 10 min, at 5–10 min intervals between 11–60 min, and every 30 min thereafter up to 180 min. The degree of spinal block was quantified as the percentage of possible effect (%PE), while the peak value observed on the blocking timeline was recorded as the maximum possible effect (%MPE). The area under the curve (AUC) values were calculated using Kineticav 2.0.1 (MicroPharm International, USA). The duration of the effect was defined as the time elapsed between drug administration and the complete recovery of function. Dose-response curves for each drug were constructed, and the SAS nonlinear program (SAS Institute Inc., Cary, NC, USA) was employed to determine the ED50 (the dose producing 50% blockade), as well as the ED25 and ED75.

RESULTS

An isobolographic analysis was conducted using four fixed ratios of nalbuphine and lidocaine combinations (1:1, 0.5:0.5, 0.25:0.25, and 0.125:0.125). Intrathecal administration of nalbuphine and naloxone resulted in motor and nociceptive blockades. The ED50 (effective dose

50) values for nalbuphine-induced motor (3.81 [3.52–4.11] μmol) and nociceptive (3.52 [3.25–3.81] μmol) blockade were higher compared to lidocaine-induced motor (1.23 [1.10–1.38] μmol) and nociceptive (1.09 [0.97–1.23] μmol) blockade. At equivalent anesthetic doses (ED25, ED50, and ED75), nalbuphine exhibited a longer duration of motor and nociceptive blockade compared to lidocaine ($P < 0.01$).

Isobolographic analysis of the interaction between nalbuphine and lidocaine revealed that the experimentally determined ED50 values did not significantly differ from the predicted additive ED50 values. Nalbuphine administered intrathecally demonstrated a dose-dependent spinal blockade. While the intensity of the spinal block induced by nalbuphine was weaker than that of lidocaine, its duration of action was notably longer.

DISCUSSION

Preclinical studies demonstrated that intrathecal nalbuphine and naloxone induce motor and nociceptive blockades. Nalbuphine is less potent than lidocaine in producing spinal block, it exhibits a longer duration of action. The addition of nalbuphine to lidocaine does not enhance efficacy beyond what is observed with the combination of two local anesthetics. Instead, the combination of nalbuphine and lidocaine results in an additive effect on spinal block. Increasing the dose of the local anesthetic extends the duration of action, and combining nalbuphine with lidocaine may serve as a strategy to mitigate potential side effects.

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