

Ciprofol as a Safer Alternative to Propofol: A Comparative Clinical Evaluation.

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Abstract: Propofol has been the cornerstone intravenous anesthetic for induction and maintenance of anesthesia for several decades due to its rapid onset, ease of titration, and favorable recovery profile. However, its clinical utility is limited by several well-recognized adverse effects, including pain on injection, cardiovascular and respiratory depression, hypertriglyceridemia during prolonged use, and the rare but life-threatening Propofol Infusion Syndrome (PRIS). These limitations underscored the necessity for a newer anesthetic agent with improved safety, better hemodynamic stability, and enhanced patient tolerability. Ciprofol, a novel 2,6-disubstituted phenol derivative structurally related to propofol, was developed to address these challenges. Early clinical studies indicate that Ciprofol provides similar anesthetic efficacy with significantly reduced injection pain, more stable cardiovascular and respiratory profiles, and a lower risk of metabolic complications. This abstract highlights the pharmacological rationale and clinical need for the introduction of Ciprofol as a safer and more patient-friendly alternative to propofol in modern anesthesia practice.

Keywords: Propofol, Ciprofol, India, uses, impact etc

I. INTRODUCTION

Need for the Introduction of Ciprofol

To Overcome the Limitations of Propofol has been the gold standard intravenous anesthetic for decades, but it also has notable drawbacks. Pain on injection A very common and distressing side effect due to the lipid emulsion vehicle. Cardiovascular depression Causes hypotension and bradycardia, especially in elderly or hemodynamically unstable patients. Respiratory depression Reduces tidal volume and respiratory rate, sometimes leading to apnea. Risk of hypertriglyceridemia Due to its lipid-based formulation during prolonged use in ICU sedation. Propofol infusion syndrome (PRIS) A rare but fatal metabolic complication during long-term high-dose use.

Therefore, there was a medical and pharmacological need to develop an agent with similar efficacy but improved safety and tolerability. Improved Pharmacodynamics and Pharmacokinetic Profile. Ciprofol (also known as HSK3486) is a novel intravenous anesthetic designed to maintain the desirable effects of Propofol (rapid onset, short recovery, smooth induction) while minimizing its limitations.

Higher potency: Ciprofol requires lower doses to achieve the same hypnotic effect.

Better hemodynamic stability: Causes less drop in blood pressure and heart rate.

Shorter recovery times: Faster clearance and lower accumulation during prolonged infusion.

Reduced Pain and Local Irritation

Clinical trials show that Ciprofol causes significantly less pain on injection compared to Propofol, thanks to its lower concentration in aqueous phase and different lipid carrier system. This enhances patient comfort and acceptability, particularly in outpatient and short-procedure settings.



Better Safety Margin

Wider therapeutic window (less respiratory and cardiovascular suppression).

Lower risk of metabolic complications during ICU sedation.

Improved tolerability in elderly and high-risk patients.

Objectives of the Study (Impact of Propofol)

1. To examine the pharmacological effects of propofol on the central nervous system, cardiovascular system, and respiratory system.
2. To analyze the clinical effectiveness of propofol as an induction and maintenance agent for anesthesia.
3. To identify the short-term and long-term side effects associated with propofol administration in different patient groups.
4. To assess the safety profile of propofol during surgical procedures and intensive care sedation.

Comparison of Ciprofol (Ciprofadol) and Propofol

Ciprofol, often misspelled as Ciprofadol, is a newer intravenous anesthetic that is structurally similar to propofol but designed to offer greater potency with improved safety margins. While both drugs act on GABA-A receptors to produce hypnosis and sedation, ciprofol requires a significantly lower dose than propofol to achieve the same anesthetic effect, making it more potent. Propofol is well known for its rapid onset and quick recovery but is often associated with notable side effects such as hypotension, respiratory depression, and pain at the injection site. In contrast, ciprofol has shown reduced cardiovascular depression, less injection pain, and a more stable hemodynamic profile in clinical studies. Both agents provide smooth induction and recovery, but ciprofol may offer a better safety profile, especially in patients vulnerable to blood pressure drops. Overall, while propofol remains the standard anesthetic worldwide, ciprofol represents a promising newer alternative with comparable efficacy and fewer adverse effects.

Detailed Comparison of Ciprofol (Ciprofadol) and Propofol with Reference to India

Ciprofol sometimes referred to as Ciprofadol is a newer intravenous anesthetic agent that has begun to gain attention in India as an emerging alternative to propofol. While “propofol is widely used across Indian hospitals”, from rural district hospitals to top private tertiary-care centers, ciprofadol is still in the “early stages of evaluation, approval, and adoption” within the Indian clinical ecosystem. Pharmacologically, both drugs act as “GABA-A receptor agonists”, producing hypnosis and sedation, but ciprofadol demonstrates “higher potency”, meaning that a smaller dose can achieve the same sedative effect as propofol. This makes it particularly relevant in resource-constrained Indian settings, where drug conservation and cost efficiency are important. Propofol use in India is extensive because it is “affordable, readily available, and included in most anesthesia protocols”. However, Indian clinicians frequently encounter several drawbacks: “hypotension, bradycardia, respiratory depression”, and “pain on injection”, which can be uncomfortable for patients. In contrast, early Indian clinical trials and observational studies indicate that “ciprofadol produces less injection pain”, better hemodynamic stability, and “reduced drops in blood pressure”, which is significant for Indian patients with high prevalence of cardiovascular comorbidities such as hypertension, diabetes, and cardiac disorders.

In the Indian context, propofol remains the “standard agent” due to its low cost and strong familiarity among anesthetists, whereas ciprofadol is still “costlier and not yet available in all hospitals”, especially rural areas. Regulatory approvals are progressing, and major Indian pharmaceutical companies are beginning to explore ciprofadol production, which may reduce prices in the future. If costs decrease and widespread distribution increases, ciprofadol could become an attractive alternative for Indian anesthesia practice, especially in surgeries involving elderly, cardiac-risk, or hemodynamically unstable patients. Overall, while propofol continues to dominate clinical usage in India, ciprofadol shows promise as a “safer and more hemodynamically stable option” for the Indian healthcare environment.

Uses of Ciprofol (Ciprofadol)

Ciprofadol is a newer anesthetic medicine, not yet widely used in India but emerging in clinical trials.

1. Induction of General Anesthesia: Used to make a patient unconscious at the beginning of surgery.

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2. Maintenance of Anesthesia: Given continuously during surgery to keep the patient asleep.
3. Sedation During Medical Procedures: Used for short procedures like:
 - Endoscopy
 - Minor surgeries
 - Diagnostic procedures
4. ICU Sedation: Helps keep critically ill patients calm or asleep when they are on ventilators.
5. Reduced Injection Pain: One major advantage is less pain during IV injection compared to propofol.
6. Better Hemodynamic Stability: Useful in patients with heart issues or low blood pressure because it causes fewer cardiovascular side effects.

Uses of Propofol

Propofol is widely used in India and across the world.

1. Induction of Anesthesia: Used to put patients to sleep before surgery.
2. Maintenance of Anesthesia: Given as a continuous infusion during surgery.
3. Sedation for Minor Procedures

Commonly used in:

- Endoscopies
- Colonoscopies
- Dental procedures
- MRI/CT scans for children and anxious patients

4. ICU Sedation: Used for patients on ventilators to keep them calm and comfortable.
5. Fast Recovery Agent: Preferred because patients wake up quickly with less drowsiness.
6. Anti-nausea Effect: Propofol reduces postoperative nausea and vomiting.

Key Characteristics and Mechanism

- Mechanism of Action: Ciprofol is a highly selective positive allosteric modulator of the gamma-aminobutyric acid type A (GABA_A) receptor in the central nervous system, enhancing the effect of the inhibitory neurotransmitter GABA.
- Potency: It is approximately four to six times more potent than propofol, meaning that lower doses are required to achieve comparable levels of sedation or anesthesia.
- Pharmacokinetics: The drug is characterized by a rapid onset of action (typically within 30 to 60 seconds) and a quick recovery profile due to rapid metabolism and distribution from the central nervous system to peripheral tissues.

Advantages Over Propofol

Clinical studies and meta-analyses suggest that ciprofol offers several advantages compared to the widely used propofol:

- Reduced Injection Pain: A significantly lower incidence of pain at the injection site, a common side effect of propofol, has been observed.
- Greater Hemodynamic Stability: Ciprofol is associated with a lower incidence of hypotension (low blood pressure) and other cardiovascular adverse events during induction and maintenance of anesthesia.
- Milder Respiratory Depression: Studies indicate that ciprofol may cause less severe respiratory depression and hypoxemia than propofol.
- Higher Patient Satisfaction: Ciprofol has been associated with higher patient and anesthesiologist satisfaction scores in some studies.



Clinical Applications

Ciprofol is used for various medical procedures and settings, including:

- Induction and maintenance of general anesthesia in adults undergoing various surgeries.
- Procedural sedation for non-operating room settings such as gastrointestinal endoscopy, colonoscopy, and fiber-optic bronchoscopy.
- Sedation of mechanically ventilated patients in intensive care units (ICU).

Recommendations

1. Ensure Use Only by Qualified Professionals Both Ciprofol and Propofol should be administered strictly by trained anesthesiologists or critical care experts, as improper dosing can cause serious respiratory and cardiovascular complications.
2. Strengthen Patient Monitoring During Administration Continuous monitoring of blood pressure, oxygen saturation, heart rate, and respiratory rate is essential to prevent adverse reactions, especially in high-risk Indian patients (elderly, diabetic, cardiac patients).
3. Promote Adoption of Ciprofol in High-Risk Patients Indian hospitals may consider using Ciprofol for patients prone to hypotension or cardiovascular instability, as it has shown better hemodynamic stability compared to Propofol.
4. Improve Availability of Ciprofol in India Pharmaceutical companies and regulatory agencies should work toward making Ciprofol more accessible in Indian hospitals, especially tertiary-care and government medical colleges, where newer agents are needed.
5. Cost-Effectiveness Studies for Indian Settings Before widespread use, India-specific cost analysis should be done, comparing Ciprofol's price and benefits with Propofol to ensure affordability in both public and private healthcare systems.
6. Reduce Injection-Related Pain for Propofol Hospitals should adopt the practice of mixing propofol with lidocaine to minimize injection pain, improving patient comfort.
7. Encourage Clinical Training on Newer Agents Workshops and CME (Continuing Medical Education) programmes should educate Indian anesthesiologists on using Ciprofol safely and effectively.
8. Prefer Propofol for Short Procedures Due to Fast Recovery For minor surgeries, endoscopies, and day-care procedures, Propofol remains the most efficient choice because of its fast induction and recovery profile.
9. Avoid Prolonged Infusion of Either Drug Without Proper Protocols Long-term infusion especially in ICU should follow strict guidelines to prevent complications such as Propofol Infusion Syndrome (PIS).
10. Encourage More Indian Clinical Trials To strengthen evidence, India should conduct more comparative trials evaluating safety, effectiveness, and patient outcomes of Ciprofol vs. Propofol across diverse populations.

II. CONCLUSION

Propofol has served as a cornerstone intravenous anesthetic for decades, yet its clinical use is constrained by well-documented adverse effects, including injection pain, cardiovascular and respiratory depression, metabolic complications, and the rare but serious Propofol Infusion Syndrome (PRIS). These limitations highlighted an urgent need for a safer, more tolerable alternative that could preserve the desirable anesthetic properties of propofol while minimizing its risks. Ciprofol, a structurally refined analog, was developed to address this gap and has demonstrated promising outcomes in early clinical evaluations. Evidence indicates that Ciprofol provides comparable anesthetic efficacy with significantly reduced injection pain, improved hemodynamic stability, and lower metabolic burden during prolonged use. As a next-generation intravenous anesthetic, Ciprofol represents a meaningful advancement in anesthesia practice, offering enhanced patient comfort and improved safety margins. Continued research, broader clinical trials, and long-term evaluations will further define its role, but current findings strongly support Ciprofol as a safer and more patient-friendly alternative to propofol in modern anesthetic care.

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