
Ciprofol- a game changing intravenous anesthetic or another experimental drug!

To the Editor,

Propofol (2,6, diiso-propoxyphenol) is undoubtedly the most popular induction agent used in anesthesia. With total intravenous anesthesia (TIVA) getting popular among many anesthesiologists, propofol occupies the place as a reliable agent for maintenance agent for surgical anesthesia, procedural sedation, and intensive care unit (ICU) sedation. The other advantages are rapid onset, rapid recovery, and a high clearance rate. The commonly encountered issues with the use of propofol are pain on injection, hemodynamic issues in elderly patients, dose-dependent respiratory depression in pediatric and elderly patients, patients with cardiovascular diseases, and hypovolemia. The other undesirable issues with the use of propofol are myoclonus and propofol infusion syndrome which leads to hyperkalemia and cardiac arrest after a prolonged infusion.

Ciprofol (working name- HSK3486) is a γ -aminobutyric acid (GABA) receptor agonist and is a novel 2,6-disubstituted phenol derivative like propofol. It is a recently introduced intravenous anesthetic agent which has undergone phase I and II trials in Australia and China. It is manufactured by

Haisco Pharmaceutical Group Co., Ltd.^[1] At a dose ranging from 0.4 to 0.6 mg/kg, ciprofol has comparable anesthetic efficacy, onset, recovery, and clearance rate after an infusion (in healthy volunteers) to that of propofol. Studies have demonstrated that pain on injection is lesser when compared to propofol possibly due to lower concentration in the aqueous phase of the emulsion. Ciprofol demonstrated favorable anesthetic properties with little residual effects in a study involving si healthy volunteers who received a dose of 0.4 mg/kg. When studied with ¹⁴C-labeled intravenous dose of ciprofol, there were circulating metabolites that were identified on analysis and were found to be nonhypnotic and nontoxic.^[2]

In a phase IIa multi-center, open-label, nonrandomized, positive control, dose-escalating study, Teng *et al.*^[3] compared 0.2–0.5 mg/kg of ciprofol with 2 mg/kg propofol for colonoscopy and found both drugs suitable and tolerable. In the same study, a phase IIb randomized trial with three groups was conducted. Two doses of ciprofol i.e., 0.4 and 0.5 mg/kg were compared with 2 mg/kg propofol. The authors concluded that at doses of 0.4–0.5 mg/kg, ciprofol induced

equivalent sedation and anesthesia with a similar safety profile to propofol 2.0 mg/kg during colonoscopy without major adverse events.

In an open-label, randomized, two-way cross-over study, involving healthy subjects conducted by Hu *et al.*,^[4] authors randomized subjects to receive initial doses of ciprofol/propofol as an infusion for 30 min in part 1 (n = 8) and a bolus dose in part 2 (n = 8) followed by maintenance infusions for a total of 4 h in part 1 and 12 h in part 2. The safety and tolerability of both drugs were comparable. The pain on injection and respiratory depression were less with ciprofol when compared to propofol.

Liu *et al.*^[5] conducted a multicenter, open-label, randomized, propofol positive-controlled, phase 2 trial involving 39 Chinese ICU patients for whom mechanical ventilation was indicated. They randomly assigned the patients to receive ciprofol or propofol group in a 2:1 ratio. Ciprofol loading was with 0.1–0.2 mg/kg for 0.5–5 min, a maintenance infusion rate of 0.3 mg/kg/h, which was adjusted to a rate of 0.06 to 0.80 mg/kg/h. Propofol loading was at 0.5–1.0 mg/kg for 0.5–5 min, a maintenance infusion rate of 1.5 mg/kg/h adjusted to 0.3–4.0 mg/kg/h. The adjustment was done to achieve an acceptable sedation score. On analysis of 36 patients who completed the study, the authors concluded that tolerability, sedation characteristics, and adverse events like hypotension were comparable between both groups with the doses used in patients on mechanical ventilation.

Propofol infusion syndrome (PIS) is a well-described syndrome that occurs due to prolonged infusion described in adults and pediatric patients.^[6] The present literature has not described anything similar to PIS with the use of ciprofol. Other off-label indications of propofol like status epilepticus and as an anti-emetic have not been explored with ciprofol yet.

To conclude, ciprofol appears to be an anesthetic agent and sedative with properties similar to propofol with lesser pain on injection and better cardiovascular stability. However, further comparative studies are required to establish its superiority or comparability to propofol.

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Conflicts of interest
There are no conflicts of interest.

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