

PROPOFOL

Use

Propofol is a rapid acting intravenous anaesthetic. Adults needing intensive care are often sedated with a continuous infusion, but serious (sometimes lethal) metabolic complications were encountered when this strategy was used in children. Pain control requires an opiate, such as remifentanil (q.v.), as well.

Pharmacology

Propofol is a clear colourless insoluble phenolic compound supplied in an isotonic, oil-in-water, Intralipid emulsion that came into use as a useful, short acting, IV anaesthetic in 1984. It is unrelated, chemically, to any other anaesthetic agent, but behaves rather like ketamine (q.v.). Recovery from propofol is, however, rather more rapid, and 'hangovers' are less common. The drug is rapidly redistributed into fat and other body tissues and more than half leaves the circulation within 10 minutes even after neonatal IV administration ($V_D \sim 4$ l/kg). It is then conjugated and metabolised in the liver, the elimination half life being 5–10 hours although, with sustained use, elimination from deep stores may take 2–3 days. Propofol is not teratogenic or fetotoxic in animals but crosses the placenta readily, and the manufacturers do not recommend use during pregnancy or delivery, although no problems have been encountered with use for Caesarean delivery. Neither has the main manufacturer yet recommended the use of propofol to induce anaesthesia in the neonate, to sustain anaesthesia in patients less than 3 years old, or to provide continuous sedation in patients under 17. Substantial quantities appear in breast milk, but a baby taking milk from the breast 12 hours after the mother's delivery under propofol anaesthesia would ingest less than 1% of the weight-related maternal dose.

The drug was used as a sedative in paediatric intensive care for 15 years before any controlled trials were undertaken, and it was several years before reports of unexpected metabolic acidosis, and rhabdomyolysis, with sudden life-threatening cardiac and renal failure started to appear. In one still unpublished control trial, in which 222 children received a sustained 1% or 2% propofol infusion and 105 some other sedative, all but 4 of the 25 deaths occurred in children given propofol. It is now clear that prolonged infusion can sometimes cause a myopathy due to impaired fatty-acid oxidation in patients of *any* age which is only reversible by stopping treatment at once and offering prompt haemoperfusion. Maintaining a generous dextrose infusion may make this hazard less likely by limiting the tendency of the body to mobilise energy stores from fat.

Use during neonatal intubation

2.5 mg/kg of propofol given IV over 10 seconds will usually cause relaxation without apnoea, and render the baby oblivious to the stress of intubation, but some babies need a second dose. The addition of a 3 micrograms/kg bolus of remifentanil (q.v.) can be used to provide pain-free working conditions within 90 seconds, but this can cause brief apnoea, and intubation on its own should cause relatively little pain.

Use for continuous IV sedation or anaesthesia

Maintenance anaesthesia: Anaesthesia for any procedure lasting more than 10–15 minutes requires a maintenance infusion of propofol. Evidence suggests that this should **never** be given to any young child at a rate exceeding 4 mg/kg per hour. Where (as is often the case) this fails to provide adequate pain relief, an opiate, such as remifentanil, should be given as well – the dose of propofol should not be increased.

Prolonged sedation: Propofol is now widely used to provide sustained sedation for patients requiring intensive care, but it should **not** be used in this way, especially in children less than three years old because there is a small, but currently unpredictable, risk of sudden 'propofol infusion syndrome' collapse.

Precautions

Propofol use must be supervised by an experienced intensivist, and recovery monitored until it is complete.

Supply and administration

20 ml ampoules of an IV emulsion containing 10 mg/ml cost £2.30. Store ampoules at room temperature, shake before use, and do not freeze. The lipid content makes it important to protect any line used for sustained infusion from microbial contamination. Do not infuse through a <1.2 μ m filter. IV injection can cause transient pain, but this can be relieved by adding 50 micrograms of lidocaine to each mg of propofol.

References

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