

# Propofol: contraindicated for sedation of pediatric intensive care patients

**Reason for posting:** Propofol — an anesthetic agent<sup>1</sup> — may cause life-threatening adverse events when used to sedate critically ill children.<sup>2</sup> The problem was first noted in 1992, when a report was published of 5 children with croup or bronchiolitis in an intensive care unit (ICU) who were sedated with propofol and subsequently died of metabolic acidosis and myocardial failure.<sup>3</sup>

Subsequently termed “propofol syndrome,” sporadic cases were described in the literature, including a report in 1998 of 18 critically ill pediatric patients who experienced bradycardia, asystole, severe metabolic acidosis, lipemia, hepatomegaly and rhabdomyolysis.<sup>4</sup> In 2001 the US Food and Drug Administration communicated that pediatric ICU patients given the drug for sedation as part of a randomized controlled trial had higher death rates than those who received standard anesthetic agents.<sup>5,6</sup> Health Canada recently reported that 6 serious postmarketing adverse events, including 3 deaths, had occurred in children receiving propofol in an ICU setting.<sup>2</sup> All patients experienced metabolic acidosis, hemodynamic instability and cardiac conduction abnormalities.<sup>2</sup> Canadian product monographs for propofol infusions are now being updated to indicate that the agent is contraindicated for the sedation of children receiving intensive care.

**The drug:** Propofol is a chemically distinct hypnotic agent administered intravenously for the induction and maintenance of general anesthesia or for sedation in both adults and children.<sup>1</sup> The rapid onset and offset of action and the relative lack of cumulative effects have made it popular.<sup>7</sup> The 2002 *Compendium of Pharmaceuticals and Specialties* states that propofol is indicated for anesthesia in children 3 years of age and older but that it is not recommended for sedation in children

under the age of 18 years, either during surgical or diagnostic procedures or in the ICU.<sup>1</sup>

Results of biochemical analyses throughout the clinical course of a pediatric patient who experienced propofol syndrome and recovered after hemodialysis suggest that impaired fatty acid oxidation at the level of the mitochondria may be responsible for this syndrome.<sup>8</sup> However, patient-specific factors predicting this adverse effect, and the reason for its relative absence in adults, are not yet known.

**What to do:** The propofol syndrome has occurred in critically ill children receiving the drug for sedation. In such patients, alternative sedatives should be used. The syndrome may be less common when the drug is used in less critically ill pediatric patients for short periods (e.g., for procedural sedation or for the induction and maintenance of general anesthesia).<sup>9,10</sup> Unfortunately, large randomized controlled trials evaluating the drug's safety for this indication are lacking.<sup>11</sup> The known and theoretical risks of propofol should be explained to parents.

Many drugs licensed for use in adults are used “off label” in children.<sup>12</sup> The serious, life-threatening postmarketing adverse events seen with propofol reinforce that significant harm can come from off-label use of agents whose pediatric safety profile is incomplete.

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