

Chloral Hydrate Safety Issues

Chloral hydrate is a sedative-hypnotic that has been associated with serious adverse events in the pediatric population including dosing errors, over-sedation, and administration of the oral liquid by the intravenous (IV) route. In 2012, commercially available chloral hydrate products were discontinued and taken off the market. However, some ambulatory and hospital pharmacies are compounding an oral suspension of chloral hydrate for pediatric sedation in both inpatient and outpatient settings. Section 503A of the Federal Food, Drug and Cosmetic Act permits pharmacists to compound chloral hydrate to provide patient specific prescriptions in limited quantities. Compounded drugs are not approved by the US Food and Drug Administration (FDA), which means the FDA does not verify the safety or effectiveness of compounded drugs. One study found that compared to the commercial formulation, the compounded drug provided a shorter duration of sedation, more frequent need for an additional sedation agent, and frequent sedation failure.

Over the last two years, there have been three reported cases of pediatric chloral hydrate overdoses and one death that occurred in the outpatient setting. Respiratory depression and arrest are two serious adverse events that can occur following chloral hydrate administration. Other risks associated with chloral hydrate use include:

- **Resedation after discharge.** Chloral hydrate can result in prolonged sedation or resedation with effects lasting longer than 24 hours in children of all ages, even if they appear to have cleared the sedation prior to discharge. Chloral hydrate is converted to trichloroethanol, which has a half-life of up to 66 hours in neonates, 28-40 hours in infants, 8-12 hours in children, and longer following an overdose.
- **No reversal agent.** There is no specific agent available to reverse the effects of chloral hydrate.
- **Narrow therapeutic index.** Chloral hydrate has a narrow therapeutic index (a very small dose range that provides benefit without causing harm), which increases the risk of adverse effects when higher therapeutic doses or overdoses are administered.
- **Cardiac toxicity and hypotension.** Large doses or overdoses have been reported to cause ventricular dysrhythmias and severe hypotension.
- **Irritating gastric effects.** Chloral hydrate is more rapidly absorbed with food; fasting before a procedure is not recommended since it can delay drug onset, resulting in inadequate sedation. Gastric irritation can occur, leading to vomiting and potential aspiration of stomach contents.
- **Large volume per dose.** Chloral hydrate is very bitter tasting and requires a large volume per dose, often requiring a nasogastric tube for administration. In addition, compounded chloral hydrate is difficult to concentrate, resulting in very large volumes per dose which can lead to vomiting.

Due to its low cost, chloral hydrate has been used widely for pediatric sedation in many facilities. However, the literature provides conflicting recommendations. Some studies suggest other sedatives such as midazolam may be more predictable and produce less severe adverse effects. Other studies have shown chloral hydrate to provide more effective pediatric sedation and should be used for painless diagnostic procedures.

Reference

Institute for Safe Medication Practices. (2016). *Nurse Advise-ERR*. Retrieved from Institute for Safe Medication Practices: <http://www.ismp.org/newsletters/nursing/issues/NurseAdviseERR201612.pdf>