

Intravenous Fat Emulsions (Intralipid™)

Intravenous fat emulsions (IFEs) have been used in patient care for several decades, as a source of calories for the malnourished and as a vehicle to deliver drugs that are poorly soluble in water including some anesthetic agents, sedatives, analgesics and antihypertensives. IFEs are oil-in-water emulsions that consist of one or more triglyceride-containing oils, a phospholipid emulsifier and glycerin. Animal studies and case reports have suggested that 20% IFEs may aid in the resuscitation of hemodynamically unstable patients as a result of an overdose of a lipophilic drug.

Mechanism/Indications: Although the exact mechanism of action of IFEs for rescue therapy is not clearly understood, the strongest evidence comes from the proposed lipid sink/sponge mechanism. Once in circulation, the emulsion acts as a sink/sponge, extracting lipophilic drug molecules. This reduces drug distribution to tissue and enhances redistribution from the tissue to the non-aqueous part of the plasma. Although most of the data relating to the use of IFEs as antidotes have come from overdoses of local anesthetics such as bupivacaine, new applications are being investigated for overdoses with other lipid-soluble substances (Table 1). For example, in a case report of severe toxicity associated with an ingestion of six grams of sustained-released verapamil, serum concentrations of the drug decreased from 2 to 0.04 µg/mL (therapeutic range 0.05 – 0.2 µg/mL) after the administration of 250 mL IFE. (*Clin Toxicol* 2010;48:646 [abstract]). Currently, IFEs should only be considered for patients with hemodynamic instability, or status epilepticus, after ingestion of a lipid-soluble substance.

Table 1. Lipid-Soluble Substances

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|------------|------------------|------------------------|-----------------|-------------|
| Amlodipine | Verapamil | Betaxolol | Bromadiolone | Bupivacaine |
| Bupropion | Carvedilol | Cyclic Antidepressants | Diphenhydramine | Flecainide |
| Metoprolol | Organophosphates | Propranolol | Quetiapine | Timolol |

Dosing: Commercially, IFE comes in a variety of strengths. The most commonly used formulation in most institutions for parenteral nutrition and toxicology is Intralipid™ 20%. The recommended adult dose for overdose of lipid-soluble substances is Intralipid™ 20% 1.5 mL/kg (lean body weight) IV bolus over 2 – 3 minutes, followed by an infusion of Intralipid™ 20% 15 mL/kg IV over 60 minutes. The bolus dose may be repeated once, as needed, if hemodynamic instability persists. Intralipid™ should be used to supplement Advanced Cardiac Life Support (ACLS) measures, as it is imperative that the IFE circulates throughout the patient once administered. Also, as the product can alter certain hematologic parameters, it is important to draw labs such as ABG, CBC, electrolytes, triglycerides and serum drug concentrations prior to dosing.

Adverse Effects/Contraindications: In general, there is a lack of safety data concerning the use of IFEs as rescue therapy. No data exists concerning the use of IFEs in children. Adverse effects associated with the use of IFEs have mostly been reported in patients receiving them as part of parenteral nutrition regimens and have included hypertriglyceridemia, acute pancreatitis, cholestasis and increased risk of infection. Rapid infusions of IFE have the potential to induce fat

Intravenous Fat Emulsions (continued)

overload syndrome, characterized by hyperlipidemia, fever, hepatomegaly, anemia, coagulation disturbances, seizures and coma. Administration of Intralipid™ 20% within the recommended daily doses and infusion rates will minimize the potential for these toxicities; however the upper limits of infusion rates as well as the maximum tolerable dose have not been established. Increased pulmonary artery pressure leading to acute lung injury (ALI) has been noted in patients with acute respiratory distress syndrome (ARDS) in whom IFEs were utilized as rescue therapy. IFEs are contraindicated in patients with hypersensitivity to any component of the formulation, or severe egg or legume (soybean) allergies.

Nicholas Fusco, PharmD
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For more on intravenous fat emulsions:

- *Bania TC. Antidotes in Depth: Intravenous Fat Emulsions. In: Flomenbaum NE, Goldfrank LR, Hoffman RS et al, eds: Goldfrank's Toxicologic Emergencies. New York NY, 2011;976-981.*
- *Mirtallo, JM, et al. State of the Art Review: Intravenous Fat Emulsions: Current Applications, Safety Profile, and Clinical Implications. Ann Pharmacother 2010; 44:688-700.*
- *Cave, G, Harvey, M. Intravenous Lipid Emulsion as Antidote Beyond Local Anesthetic Toxicity: A Systematic Review. Acad Emerg Med 2009; 16:815-824.*
- *www.lipidrescue.org*
- *Armenian P, French D, Smollin C, Olson K, Wu AHB. Prolonged Absorption from Sustained-Release Verapamil Preparation with Documentation of Serum Levels and Their Response to Intralipids. Clin Toxicol 2010; 48(6):646 (abstract)*

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