

# Use of Intravenous Lipid Emulsions for Treating Certain Poisoning Cases in Small Animals

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## KEYWORDS

- Poisoning • Antidote • Lipid emulsion • Intralipids
- Fat emulsion • Intoxication

The use of intravenous (IV) lipid emulsion (ILE; Intralipids, Liposyn, Medialipid) in the resuscitation of human patients poisoned by accidental local anesthetic overdoses has become a common practice in the human medicine arena over the past decade.<sup>1</sup> More recently, ILE therapy has been used in the veterinary world for the management of a variety of toxicoses.<sup>2</sup> Although further clinical studies are needed to determine the safety and effectiveness and risk:benefit ratio of this modality, a growing number of experimental studies and case reports suggest that ILE may become valuable addition to the veterinary clinician's emergency drug arsenal.

ILE is composed of neutral, medium to long-chain triglycerides derived from combinations of plant oils (eg, soybean, safflower), egg phosphatides, and glycerin. Formulated primarily a source of essential fatty acids for patients requiring parenteral nutrition, ILE is available in formulations ranging from 10% to 30% lipid; the latter is for compounding use and not for direct infusion.<sup>3</sup> ILE is stored at room temperature, and an unopened container will have a shelf life of up to 2 years.<sup>2,3</sup> Once opened and/or mixed with other fluids, ILE should be refrigerated between uses and used within 24 hours.<sup>3</sup> ILE can be administered via peripheral or central venous catheter.<sup>3</sup> ILE have a high margin of safety, with an estimated IV LD<sub>50</sub> in rats of 67 mL/kg.<sup>5</sup>

## BACKGROUND

The use of ILE as an antidotal procedure evolved from the discovery that administration of lipid solutions could attenuate the cardiotoxicosis of bupivacaine in rats.<sup>6</sup> A study in dogs demonstrated that IV overdoses of bupivacaine (10 mg/kg) resulted in

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deaths in all dogs receiving open-chest cardiac massage but no deaths in dogs receiving open-chest cardiac massage along with infusion of 20% ILE.<sup>7</sup> Although one porcine model failed to show similar positive benefits of ILE in bupivacaine,<sup>8</sup> there were concerns expressed regarding the cardiac effects of anesthetic drugs used on the pigs prior to administration of cardiotoxic levels of bupivacaine.<sup>9</sup> Another study performed on pigs showed that ILE reversed bupivacaine-induced cardiac electrophysiologic abnormalities.<sup>10</sup> Based on these results, it was proposed that ILE may be a potentially useful treatment for local anesthetic systemic toxicosis (LAST) in humans, a condition that tends to be resistant to conventional modes of resuscitation.<sup>1</sup>

Subsequently, numerous human case reports emerged showing positive results of the use of ILE in resuscitation of patients experiencing the cardiac effects of LAST. In one case, an elderly woman received 3 bupivacaine injections for peripheral and spinal nerve blocks.<sup>11</sup> Three minutes after third injection, she became nonverbal and had a seizure. The patient received 1.5 mL/kg of ILE within 2 minutes and seizure activity ceased; she regained consciousness within 3–4 minutes. In another case, a 17 year-old adolescent male experienced seizures and became pulseless after receiving 20 mL of 0.5% bupivacaine for postoperative analgesia.<sup>12</sup> He was treated with midazolam and 8 mL/kg of 20% ILE. The patient's cardiac status normalized following ILE infusion. In a final case, a 58 year-old man developed a tonic-clonic seizure 30 seconds following injection of bupivacaine for a brachial plexus nerve block.<sup>13</sup> Asystole occurred 90 seconds later; following 20 minutes of unsuccessful chemical, mechanical, and electrical attempts at resuscitation, the patient was being prepared for cardiopulmonary bypass when ILE was suggested. Within a few seconds of initiation of administration of 20% ILE, a single sinus beat appeared and progressed to normal sinus rhythm within 15 seconds. The patient fully recovered with no adverse effects.

Despite these and several similar cases, the use of ILE for LAST remained controversial due to the inability to demonstrate conclusively that ILE, and not adjunctive resuscitation measures (cardiac compression, electroconversion, other drugs, etc), were responsible for the recoveries.<sup>14,15</sup> Critics have also pointed out that the case reports reflected only those cases in which the ILE treatment was successful, noting that unsuccessful treatments did not merit reporting, so the actual efficacy of ILE therapy was not known. Criticisms aside, sufficient evidence of the potential of ILE to result in a positive outcome in LAST patients existed such that this treatment modality has been recommended for management of LAST by a number of human medical organizations, including the Association of Anaesthetists of Great Britain and Ireland, the American Society of Critical Care Anesthesiologists, the American Society of Anesthesiologists Committee on Critical Care Medicine, the Resuscitation Council of the UK, and the American Society of Regional Anesthesia.<sup>1</sup>

Recognizing that randomized controlled trials may not be possible given the catastrophic nature of situations where ILE are used in human intoxications, an international collaboration of clinical investigators has developed an online registry (<http://www.lipidregistry.org>) for reporting cases where ILE has been used antidotally.<sup>1</sup> This LIPAEMIC (Lipid Injection for the Purpose of Antidotal Effect in Lipophilic Medicine Intoxication) Study Group is attempting to collate clinical experiences of efficacy and adverse events associated with the antidotal use of ILE. Additionally, physicians and veterinarians can post their experiences with ILE as an antidote on the "Lipid Rescue" website (<http://www.lipidrescue.org>).

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