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Intravenous lipid therapy for toxin cases: “The gift of the glob”

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A novel and promising development in toxicology is the use of intravenous lipid emulsions as an antidote for some fat soluble toxins. Lipid emulsions are the fat component of parenteral nutrition, and they have been used for this purpose in clinical practice for many years. In 1988, a physician investigating the adverse cardiovascular effects of bupivacaine chanced upon the discovery that rats treated with intravenous lipids were resistant to cardiovascular collapse induced by toxic doses of bupivacaine. He did further laboratory research, much of it with dogs, and demonstrated that dogs given intravenous lipid therapy after cardiac arrest from bupivacaine could be easily resuscitated, while those that did not receive lipid therapy died despite aggressive resuscitation efforts. These intriguing findings initiated a cascade of further research exploring how intravenous lipid emulsions exert a therapeutic effect. Lipids were demonstrated to be an effective antidote to toxic doses of other drugs, such as bupropion, lamotrigine and verapamil. Physicians began reporting the often dramatically successful use of intravenous lipid therapy to treat non-bupivacaine drug toxicities in emergency settings.

The mechanism by which intravenous lipid therapy assists in reversing toxicities of a wide range of pharmaceuticals has not been conclusively determined, but most evidence points to the “lipid sink” hypothesis. According to this theory, a bolus infusion of a lipid emulsion into the plasma provides a lipid compartment into which a toxin may diffuse down a concentration gradient from target tissue sites, such as the brain or cardiac parenchyma. This hypothesis was generated by the observation that intravenous lipid therapy appears to be more effective for highly lipid-soluble drugs than for water soluble substances. Further, the principal researcher demonstrated that radiolabeled bupivacaine added to lipid-treated rat plasma partitions into the lipid component. Intravenous lipid therapy is now standard emergency therapy for bupivacaine toxicity in human medicine and is increasingly considered for life-threatening toxicities of other lipid-soluble drugs.

A puppy with severe moxidectin toxicity requiring mechanical ventilation was treated successfully with intravenous lipid therapy here at the VEC in 2009. Shortly after administration of lipid therapy, the pup resumed spontaneous respiratory efforts, and went on to recover fully within hours rather than the expected time period of several days. This case, published in the Journal of Veterinary Emergency and Critical Care, was the first toxin case report to introduce the concept of lipid therapy to the veterinary emergency community. Subsequently, a case report has been published on use of intravenous lipid emulsion for ivermectin toxicity and many anecdotal reports swirl around VIN on the use of lipids for baclofen, pyrethrin toxicosis, moxidectin and ivermectin. More recently, we used lipid emulsion to successfully treat a young dog with baclofen overdose. The dog developed seizures and paralysis after ingesting a toxic dose of baclofen, a commonly used muscle relaxant. The patient arrested within minutes of arriving at the VEC, but was successfully resuscitated. Lipid therapy appeared to assist in the rapid recovery of spontaneous ventilation, and the dog recovered fully within 3 ½ days.

There are many questions yet to be answered regarding lipid therapy. Recommendations regarding dosing, efficacy, timing and case selection are evolving. While intravenous lipid therapy appears to be safe based on use in humans and a handful of anecdotal reports in veterinary medicine, there is insufficient data to establish the true risks of therapy. Pancreatitis and fat embolism are potential concerns. Currently, lipid therapy is not recommended for non-life-threatening toxins that can be safely treated with conventional therapy. Cases presenting with life-threatening clinical signs secondary to lipid-soluble toxins may be considered for the experimental treatment of lipid therapy. In the veterinary environment, moxidectin, ivermectin, baclofen, beta-blockers, calcium channel blocking drugs and of course bupivacaine are among a few toxins that may be candidates for intravenous lipid therapy.

We are proud to have been at the forefront of introducing this innovative therapy to the veterinary community. I follow the human and veterinary literature on intravenous lipid therapy with interest, keeping an eye on how we can best use it to treat the toxin cases presenting to our emergency service. For more information, see www.lipidrescue.org, or the references below. As always, Dr. Brown and I are happy to accept direct referrals of critically ill patients. “After hours” we are always available to the ER service clinicians for consultation on critically ill patients, and will assume primary care when in the clinic.

References:
Crandell DE, Weinberg GL. Moxidectin toxicosis in a puppy successfully treated with intravenous lipids. J Vet Emerg Crit Care (San Antonio) 2009; 19(2):181-186
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Rothschild L et al. Intravenous lipid emulsion in clinical toxicology. Scand J Trauma Resusc Emerg Med 2010; 18(51)

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