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HOW I TREAT… MAJOR INTOXICATIONS WITH INTRAVENOUS LIPID EMULSION (IVLE)?

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The use of intravenous lipid emulsions (ILE) for certain intoxications has been standard practice in in human medicine over the last 10-15 years. More recently it has become a common therapy for management of specific intoxications in small animal medicine as well. This lecture will serve to review how ILE works, which intoxications it can be considered for, and the practicalities of administration with potential side effects

MECHANISM OF ACTION

The mechanism of action in which lipids in prove the clinical signs of toxicity in not precisely know. There are two current theories for the antidotal effects of ILE and it is likely that there may be more than one mechanism, or that there may be different mechanisms depending on the toxin ingested. The first theory is that lipids can increase cardiac performance which likely plays a role in toxins like the local anesthetics causing cardiovascular collapse. The other major theory is that they can act as a "lipid sink" for the intoxicant sequestering it in the lipid compartment of the blood.

One potential mechanism for improved cardiovascular performance is that free fatty acids are the preferred energy source for myocardial mitochondria. The local anesthetics such as bupivacaine in toxic doses can block mitochondrial ATP production and by providing free fatty acids directly to the muscle. Alternatively there is some evidence that ILE can increase intracellular calcium within cardiac myoctes. This is likely related to free fatty acid activation of myocardial calcium channels.

The alternative mechanism proposed for lipid soluble intoxicants is that by increasing the amount of lipid in the blood stream, a gradient has been created to "draw" the toxin from the tissues into the blood where it binds to the lipid. This lipid-toxin complex then distributes throughout the body and is cleared by skeletal muscle, splanchnic vicsera and subcutaneous tissues. This is the likely mechanism for lipophilic drugs which are defined by a log P value of greater than 1. Table 1 lists drugs that have the potential to be reversed by the administration of ILE along with their Log P value. Table 2 is a compilation of intoxication in which ILE has been reported in either cats or dogs clinically. All reports show a presumptive benefit except for ivermectin. This seemingly positive response to lipid therapy was not appreciated in three dogs that were homozygous for the ABCB1-1Δ gene mutation, but an effect was appreciated in a dog that did not have the mutation in the MDR gene.

Drug	Log P value
Amlodipine	1.90
Baclofen	1.30
Bupivicaine	3.64
Carprofen	4.13
Diazepam	2.82
Digoxin	1.26
Diltiazem	2.80
Itraconazole	5.90
Ivermectin	3.50
Ketoprofen	3.12
Lidocaine	2.26
Moxidectin	1.88
Naproxen	3.18
Trazadone	1.80
Vinblastine	3.69

Table 1: Lipid soluble drugs that my be able to be reversed with ILE
From Fernandez et al. JVECC 2011 (4)309-320

Dogs
- Naproxen
- Ibuprofen
- Baclofen
- Ivermectin (variable success)
- Moxidectin
- Diltiazem
- Marijuana

Cats
- Permethrin
- Ivermectin
- Lidocaine

Table 2: Toxins in which ILE has been reported to be used in the veterinary literature.

POTENTIAL SIDE EFFECTS

Although lipid solutions have been used in parenteral nutrition safely, there is no clinical evidence on safety of short-term large boluses of lipid solutions. Short-term infusions of soybean oil based lipid emulsions have been shown to decrease neutrophil function in dogs. Other potential adverse effects are pancreatitis, fat emboli, phlebitis, and hypersensitivity reactions. However, no adverse outcome related to intravenous fat emulsion therapy for the treatment of intoxication has been reported except laboratory difficulty in analyzing lipemic blood samples.

ADMINISTRATION

The optimal dose of intravenous lipid is unknown. Various reports have used a variety of quantities given over different rates. The most common dose in veterinary reports are of 1.5 ml/kg bolus (typically over 1-2 minutes) then 0.25 ml/kg/min for 30-60 minutes. A review of lipid emulsions to treat local anesthetic toxicity in humans suggests a dose of 1.5 ml/kg bolus that can be repeated up to 3 times in cardiac arrests then 0.25-0.5 ml/kg/min. On this basis it is reasonable to use this dose in veterinary medicine as well until further studies show an optimal dose.

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