Drug overdoses and serious adverse effects caused by medications can be difficult to treat. Conventional symptomatic and supportive care and Advanced Cardiac Life Support therapies may be ineffective, and even if an antidote is available, the amount of medication taken or administered and/or the patient’s clinical condition may prevent an antidote from working. In these situations, intravenous lipid therapy may be the only useful treatment.

Intravenous lipid emulsion is an accepted therapy for the treatment of severe cardiac toxic effects caused by local anesthetics. Lipid emulsion therapy has also been used successfully to treat cardiac arrest and intractable arrhythmias caused by overdoses of antiepileptic drugs, cardiovascular drugs, and psychotropic medications, but experience with intravenous lipids as antidotal therapy in these clinical situations is limited. However, intravenous lipids are relatively safe, widely available, and easy to administer, and many published case reports document their dramatic effectiveness. Patients who have not responded to standard therapies have been quickly revived by administration of intravenous lipids. Use of lipids most likely will increase, and critical care nurses should be familiar with lipid therapy. (Critical Care Nurse. 2014;34[5]:62-67)
The first reported cases in which intravenous lipid emulsion was used to treat intentional drug overdose were published in 2008. These cases (an overdose of bupropion and lamotrigine and an overdose of a β-blocker) were similar to the previously mentioned case of systemic toxic effects caused by local anesthetic. Both patients experienced cardiac arrest resistant to standard therapy, but an intravenous infusion of lipid emulsion quickly restored pulse and blood pressure, and the patients survived. Since then this treatment, often called lipid rescue therapy, has been used successfully to treat intentional overdoses of antiepileptic drugs, cardiovascular drugs, and psychotropic medications.4,9

Treatment with lipid emulsion has clearly been effective in certain clinical situations and may be useful as an emergency therapy for drug overdoses. However, the basics of this treatment— when to use it, what patients should receive it, how effective it is, and what are the possible adverse effects—have not been completely outlined. Several reasons account for these uncertainties. Information on the clinical experience with intravenous lipid as a treatment for drug overdose is limited to case reports. The evidence supporting the use of lipid for treating toxic effects due to local anesthetics is good, and the treatment is approved for this use by several professional organizations, but the evidence is mostly anecdotal, and no large randomized, controlled trials can be done to evaluate the effectiveness and safety of lipids for this clinical problem. The mechanism of action of lipid as an antidote is not completely understood. The optimal dose and how long lipid can be used is not known. The amount of clinical experience is relatively small, so the adverse effects of lipid therapy are not completely understood, and use of the therapy is still evolving. Few clinicians have experience in using lipid emulsion as emergency therapy in infants and children. A 20% lipid solution is used, but other formulations are available; the use of a 20% solution appears to be simply convention. Further experience may show that 10% or 30% is more effective. Finally, how lipid emulsion should be used in conjunction with other rescue drugs and antidotes is not clear.

What Is Intravenous Lipid?

Intravenous lipid is an emulsion of egg phospholipids and soybean oils in water that is commonly used as a source of fat, nutrients, and calories for patients who cannot tolerate oral intake. Intravenous lipid is available in 10%, 20%, and 30% solutions and in unit doses of 100, 250, 500, and 1000 mL. (Intravenous lipids are commonly called intralipids. Intralipids is a registered trademark.) The intravenous lipids currently available are manufactured and sold for use as parenteral nutrition. Antidotal therapy with intravenous lipid is considered an unlabeled use of the product.

Mechanism of Action

The mechanism of action of intravenous lipid as an antidote is not known, but the evidence from experiments in animals suggests 2 likely possibilities. The first possibility is that intravenous lipids act as a lipid sink. Lipids have been used successfully to reverse toxic effects caused by drugs and toxins that differ widely except for one factor: a high degree of lipid solubility.5 Drugs or chemicals with a high degree of lipid solubility are easily absorbed by or easily attached to lipids but are not absorbed by water. The practical effect of this characteristic is that a highly lipid-soluble drug or chemical will not remain in the intravascular compartment but will pass through cell membranes and reach binding sites in the tissues. A bolus of intravenous lipid may provide an intravascular lipid sink that attracts and absorbs highly lipid-soluble drugs or chemicals before they reach the tissues, or the lipid will actively pull drugs or chemicals from tissue binding sites.5

The second possibility involves fatty acid metabolism. Under normal circumstances, the myocardium uses fatty acids for energy. Local anesthetics inhibit fatty acid metabolism in the heart, and experiments in animals11,12 have indicated that intravenous lipid may reverse the cardiac toxic effects caused by high doses of bupivacaine by providing an exogenous energy source for the myocardium.
These 2 mechanisms of action are the ones mentioned most often in discussions of lipids as an antidote. Intravenous lipid may also be a positive inotrope, may counteract drug-induced inhibition of cardiac ion channels, or may have an effect on carnitine transport, which in turn can improve utilization of fatty acids by the heart. Clinical evidence for the antidotal mechanisms of intravenous lipid emulsion is still being accumulated, and lipids might work in different ways in different clinical situations.

Intravenous Lipid as an Antidote: Successful and Unsuccessful

As mentioned previously, intravenous lipid emulsion has been used successfully to treat systemic toxic effects caused by local anesthetics, antiepileptic drugs, cardiovascular drugs, and psychotropic drugs. In these cases, serious cardiovascular toxic effects that did not respond to standard therapies or antidotes were reversed by intravenous lipid emulsion. Several examples of these cases are as follows:

- A 17-year-old girl was found at home unresponsive. Five hours earlier, she had taken 7.95 g of bupropion and 4 g of lamotrigine. Several hours after arrival in the emergency department and 10 hours after the ingestion, she had a tonic-clonic seizure and experienced pulseless ventricular fibrillation and ventricular tachycardia. Advanced Cardiac Life Support measures were started, but the patient did not regain blood pressure, pulse, or a normal cardiac rhythm for more than a few minutes at a time. After 52 minutes of resuscitation attempts, 100 mL of a 20% lipid solution was given intravenously. One minute later, a sustained pulse was palpable, and within 15 minutes a sinus rhythm was restored. Several weeks later the patient was discharged, albeit with a mild level of neurological impairment.

- A 33-year-old woman who had taken an overdose of the calcium channel blocker felodipine, but use of lipids was successful in resuscitating patients who had taken overdoses of verapamil or a tricyclic antidepressant. In addition, a review of the use of intravenous lipid indicated that some hemodynamic parameters were not improved by lipid infusion.

No unsuccessful attempts of using lipid to reverse toxic effects caused by local anesthetics have been reported. However, intravenous lipid emulsion has not been universally successful in resuscitating patients who have taken an overdose. Lipid was not effective in resuscitating a 33-year-old woman who had taken an overdose of the calcium channel blocker felodipine, but use of lipids was successful in resuscitating patients who had taken overdoses of verapamil or a tricyclic antidepressant. In addition, a review of the use of intravenous lipid indicated that some hemodynamic parameters were not improved by lipid infusion.

Using Intravenous Lipid as an Antidote

Therapies are started and medications are administered when signs and symptoms indicate their use and with consideration of the patient’s age, medical history, and current clinical condition. In simpler terms, clinicians decide when and to whom a medication or treatment should be given.

However, for intravenous lipid, little information is available to guide this decision process. Intravenous lipid infusions have rapidly reversed life-threatening cardiac toxic effects in situations in which patients have not responded to an Advanced Cardiac Life Support protocol and other antidotal therapies have been unsuccessful.
and the temporal association between the infusion of lipids and restoration of vital signs strongly suggests that for these patients the lipids worked. Still, lipids have also been unsuccessful in attempts to resuscitate patients, and these instances of no success have occurred in clinical situations that are in many ways indistinguishable from those of the successful cases.

Unfortunately, the clinical experience with intravenous lipid as an emergency antidote is limited to a small number of case studies, and these case studies differ from each other in important ways: the patients differed in the medications they took, in age, in medical histories, in time to manifestation of toxic effects, and so on. The only similarity the successful cases share is that the drugs that were ingested or administered are highly lipid soluble. Because of these limitations and lack of knowledge, a reasonable approach to the use of intravenous lipids is as follows.

- Intravenous lipids can be used as antidotal therapy to reverse serious, systemic cardiovascular toxic effects caused by local anesthetics. The evidence for the effectiveness of lipids in this clinical situation is good, and at this time no unsuccessful attempts have been reported. In these clinical situations, acidosis and hypoxia should be corrected before the lipids are administered.5
- Intravenous lipids can be considered for use as an antidote for serious, life-threatening cardiovascular toxic effects caused by overdose with antiepileptic drugs, cardiovascular drugs, and psychotropic medications if all other therapies have been unsuccessful.
- A 20% lipid emulsion should be used. An initial dose of 1.5 mL/kg should be infused as a bolus over 5 minutes. Then a continuous infusion of 0.25 mL/kg should be administered over 30 to 60 minutes.20 The bolus can be repeated up to 3 times and/or the infusion rate can be increased if the blood pressure decreases.9

Lipids have been used to treat neonates, children, and adolescents, but only 14 cases of the use of lipids in infants and children have been reported.21,22

Other clinical concerns exist for using lipid as an antidote. The appropriate time to use it as antidotal therapy to treat a drug overdose is not known. Lipid might be harmful to cardiovascular function if the emulsion is administered when the patient is hypoxic.23,24 Lipid could also possibly interfere with the effectiveness of other medications used during resuscitation attempts if the lipids and these medications are used concurrently.4,25,26 In certain circumstances, use of lipid may increase the absorption of oral lipophilic drugs. Delayed toxic effects, possibly caused by sequestering and reabsorption of amitriptyline in the intravenous lipid, have been reported.27

### Adverse Effects of Intravenous Lipid When Used as an Antidote

The following adverse effects have been reported. Some were clearly caused by the lipid infusion, some were temporally associated with lipid administration, and some were simply reported after the use of lipids.

- Interference with laboratory studies: Intravenous lipids cause lipemia, and so the results of laboratory tests may be false or the specimens may be difficult to analyze. Lipids can interfere with determination of complete blood cell counts and measurements of serum alanine aminotransferase, albumin, amylase, bilirubin, creatine kinase, creatinine, electrolytes, glucose, lipase, magnesium, phosphate, and total protein.28-30 The interference with laboratory testing can persist up to 24 hours after administration of the lipid.31
- Pancreatitis: Several possible cases of pancreatitis (temporally associated with the administration of intravenous lipids) have been reported.28,32 The patients did not have adverse effects or require treatment. Pancreatitis associated with lipid infusion is most likely to occur if the patient has received multiple doses or a prolonged infusion of lipid.
- Lung injury: Several cases of lung injury after the use of intravenous lipid as an antidote have been reported.6,19
- Recurring toxic effects: Recurring and delayed toxic effects have been reported.27,33
- Other adverse effects: Acute renal failure, deep vein thrombosis, and digit amputation have been reported.19

### Conclusion

Intravenous lipid emulsion is an accepted treatment for serious systemic toxic effects caused by local anesthetics that are unresponsive to other therapies. Intravenous lipid has been used successfully to treat
systemic toxic effects caused by antiepileptic drugs, cardiovascular drugs, and psychotropic medications that are unresponsive to other therapies, but the clinical experience in these situations is limited to a small number of case reports. The possible adverse effects of lipid rescue therapy are not clearly known, the optimal dosing and the optimal time to give lipid is not known, and whether or not lipid interferes with other medications used during resuscitation is not known. Because of these uncertainties, intravenous lipid emulsion should not be considered a harmless magic bullet. But if a patient has taken an overdose of a medication for which lipid therapy is effective, if the patient has severe systemic cardiovascular toxic effects, and if the patient has not responded to Advanced Cardiac Life Support protocols and/or antidotal therapy, an intravenous infusion of lipid would be appropriate, and the infusion might save the patient’s life.

For more information about intravenous lipid as an antidote, visit www.lipidrescue.org. CCN

Financial Disclosures
None reported.

References