



<http://dx.doi.org/10.1016/j.jemermed.2014.10.009>

Clinical Review

INTRAVENOUS LIPID EMULSION IN THE EMERGENCY DEPARTMENT: A SYSTEMATIC REVIEW OF RECENT LITERATURE

Dazhe Cao, MD,*† Kennon Heard, MD, PHD,† Mark Foran, MD, MPH,‡ and Alex Koyfman, MD§

*Rocky Mountain Poison and Drug Center, Denver Health and Hospital Authority, Denver, Colorado, †Department of Emergency Medicine, University of Colorado School of Medicine, Aurora, Colorado, ‡Department of Emergency Medicine, New York University School of Medicine, Bellevue Hospital Center, New York, New York, and §Department of Emergency Medicine, University of Texas at Southwestern Medical Center and Parkland Memorial Hospital, Dallas, Texas

Reprint Address: Dazhe Cao, MD, Rocky Mountain Poison and Drug Center, Denver Health and Hospital Authority, 777 Bannock MC 0180, Denver, CO 80204

Abstract—Background: Intravenous lipid emulsion (ILE) has been broadly attempted in the resuscitation of neurologic and cardiac toxic drug overdoses, however, the role of ILE in the emergency department is poorly defined. **Objective:** This review aims to identify recent literature on the use of ILE in humans as an antidote and to familiarize emergency providers with the indications, availability, dosing recommendations, and adverse reactions associated with ILE use. **Methods:** A systemic literature search of MEDLINE, EMBASE, and major toxicology conference abstracts was performed for human cases using ILE as an antidote with documented clinical outcomes through January 2014. **Results:** Ninety-four published articles and 40 conference abstracts were identified, 85% of which had positive outcomes. The most common indication for ILE was for local anesthetic systemic toxicity (LAST). The most common nonlocal anesthetic xenobiotics were tricyclic-antidepressants and verapamil. **Discussion:** No standard of care is defined for the use of ILE, although the American Heart Association recommends use in LAST, and the American College of Medical Toxicology recommends consideration for circumstances of hemodynamic instability resultant from lipid-soluble xenobiotics. ILE should be administered per American Society of Regional Anesthesia and Pain Medicine dosing recommendations. Laboratory interference, pancreatitis, respiratory distress syndrome, and interference with vasopressors should be considered as risks but are uncommon. **Conclusions:** In the setting of severe hemodynamic compromise by lipid-soluble

xenobiotics, ILE may be considered for resuscitation by emergency physicians. As such, ILE may be stocked in emergency departments in close proximity to resuscitation rooms and areas where local nerve blocks are performed. © 2014 Elsevier Inc.

Keywords—Lipid emulsion; overdose; lipid solubility; resuscitation

INTRODUCTION

Intravenous lipid emulsions (ILE) have been used for decades as parenteral nutrition with Food and Drug Administration (FDA) indications for caloric supplementation and essential fatty acid deficiency. Lipid emulsion is also used as a carrier for lipid-soluble medications, most notably propofol. The benefits of lipid emulsion for bupivacaine poisoning was first suggested in a rat model by Weinberg et al in 1998 (1). The subsequent study in dogs by Dr. Weinberg and the first report of use in humans by Rosenblatt et al. in 2006 have brought about a paradigm shift in the management of acute local anesthetic toxicity toward utilization of ILE (2,3).

OBJECTIVE

The goal of the review is to summarize indications for administration of intravenous lipid emulsion in the

emergency department for acute poisoning by reviewing the current evidence supporting the use of ILE in humans and providing detailed guidelines for how to administer ILE. After reading this review, an emergency physician will be familiar with the indications, availability, administration, and common adverse reactions associated with ILE use for overdose/poisoning.

CASE PRESENTATION

A 23-year-old female presented to the emergency department by ambulance after a reported intentional ingestion of verapamil. The patient was minimally responsive with heart rate of 56 beats/min and blood pressure of 89/36 mm Hg. Shortly after arrival, providers were unable to palpate a pulse. High-quality cardiopulmonary resuscitation was initiated, and advanced cardiac life support measures were provided, including atropine, calcium, and epinephrine, without return of spontaneous circulation. High-dose insulin 1 U/kg was given as a bolus and continued as an infusion at 1 U/kg/h. At that point, the patient had been in pulseless electrical activity for > 10 min.

Clinical Questions

- What is the evidence supporting the use of ILE in this patient?
- For what poisonings should emergency department providers consider the use of ILE?
- How should ILE be administered?
- What are reported and potential adverse effects of ILE?
- How does ILE adversely impact laboratory monitoring?
- What are the considerations for stocking ILE in emergency departments?

METHODS

MEDLINE and EMBASE searches were performed from 1950 and 1974, respectively, to January 2014. MEDLINE search strategy used a combination of the following MESH terms and keywords of [*Fat Emulsion, Intravenous OR intralipid*] AND [*Drug Toxicity OR Poisoning OR overdose*]. Emtree search used query terms *lipid emulsion* AND *toxicity and intoxication* with inclusion of articles, article in press, conference paper, conference review, editorial, erratum, letter, note, review, short survey, human, and EMBASE. Search results were further narrowed by reviewing titles and abstracts by two reviewers (DC and KH). Inclusion criteria were human cases; ILE administered as an antidote in acute over-

dose, poisoning, or intoxication; and outcome (clinical response or survival) reported. Case series, retrospective studies, and prospective studies were excluded if clinical outcomes were not described for each separate case. Literature regarding lipid formulation of amphotericin was also excluded. Additional missing case reports were identified by reviewing references of review articles and bibliography found on www.lipidrescue.org. Abstracts that reported research not identified during our literature review from major toxicology meetings of the European Association of Poison Centers and Clinical Toxicologists, of the North American Congress of Clinical Toxicology and of the American College of Medical Toxicology (ACMT) were identified by search terms of *lipid* or *fat* for the years from 2006 to 2013 for reports of ILE as an antidote for acute toxicity by two reviewers (DC and KH) (4–15). Disagreements in article and conference abstract identification were resolved by mutual discussion.

The outcomes were deemed positive by cardiovascular response if the patient had return of spontaneous circulation, resolution of dysrhythmia, or increase in blood pressure; and by central nervous system response if the patient had increased consciousness or resolution of seizure. Adverse events were tracked for laboratory interference (including inability to measure, false-positive or false-negative values), pancreatitis (including clinical or imaging diagnoses and elevation in amylase or lipase), and acute respiratory distress syndrome (including pulmonary edema).

Literature Review Results

Our search strategy identified 547 potential articles (Figure 1). Reviewers agreed on 140 articles that met the first two inclusion criteria for detailed analysis. Thirty-two articles were duplicated, and eight articles could not be obtained at the study institution. Of the remaining articles, 20 articles failed to report outcomes and were excluded. Eighty articles were reviewed in the analysis of human case reports for the use of ILE as a rescue agent. An additional 13 articles were identified through review of references and bibliography on www.lipidrescue.org. One final article with two cases was identified through posting on a toxicology blog site after the systemic review process in February 2014 (16). From 2006 to 2013, forty-seven conference abstracts from major conferences in toxicology mentioned use of lipid therapy (Figure 2). Seven abstracts had since been published as manuscripts; the abstracts were excluded as duplicates.

See Table 1 for list of therapies with human case reports showing positive and negative studies and categorization by class of drugs and lipophilicity drugs

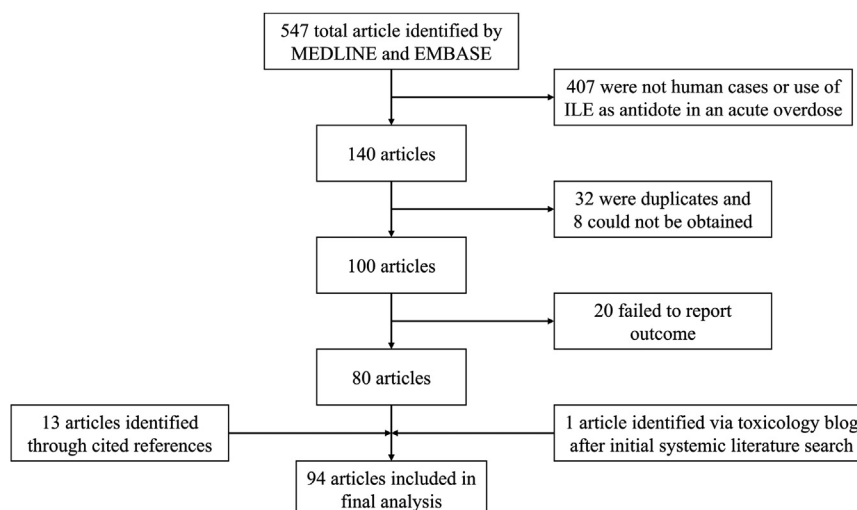


Figure 1. Flow diagram of article identification. ILE = Intravenous lipid emulsions.

(octanol:water partition coefficient, log P), where values of log $P > 2$ are considered lipid soluble and may benefit from lipid therapy based on the partitioning theory described here (17–19).

DISCUSSION

Lipid Emulsions

Lipid emulsions have been described using many different terminologies—intravenous lipid emulsion, lipid emulsion therapy, lipid resuscitation therapy, lipid rescue, intravenous fat emulsion, and Intralipid® (Fresenius Kabi, Uppsala, Sweden), which is a brand name that has become synonymous with ILE, as it is the predominant lipid emulsion used in the United States. ILE is primarily used in the isotonic 20% concentration. Lipid emulsions containing similar constituents from other manufacturers have also been used in case reports including Liposyn® III (Hospira, Lake Forest, IL), Medialipid (Medialipid, Braun, Melsungen, Germany), SMOFlipid™ (Fresenius Kabi, Mississauga, Ontario), and ClinOleic (Baxter International Inc, Mississauga, Ontario) (20). The latter three are not currently available in the United States.

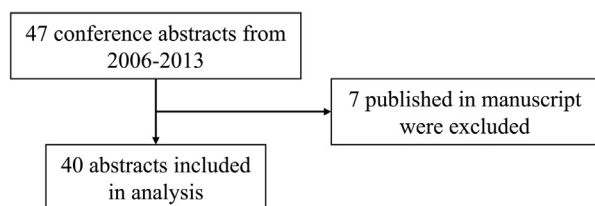


Figure 2. Flow diagram of toxicology conference abstract identification.

Proposed Mechanisms

Although numerous mechanisms for the resuscitative effects of ILE have been proposed, two theories are predominant: partitioning and enhanced cardiac metabolism. Both theories developed out of the evidence demonstrating the efficacy of lipid therapy acts across a spectrum of xenobiotic classes, each with different receptor specificities. Thus, lipid therapy mediates antidote activity either by a mechanism independent of receptor binding or via a common downstream pathway.

The partitioning theory, or lipid sink theory, postulates that the administration of lipids compartmentalizes the offending xenobiotic into lipid phase and away from the target receptors. The xenobiotics with high lipid solubility (defined as log $P > 2$) favor the lipid partition and leave the serum. Lower serum concentrations facilitate the removal of the offending agent from tissues by the generation of a concentration gradient (21–23). Weinberg et al. demonstrated enhanced myocyte clearance of radiolabeled bupivacaine after lipid infusion and accelerated recovery from asystole (23). Although the bupivacaine concentration was not explicitly measured in the lipid phase, the authors presumed the “wash out” of bupivacaine by the introduction of a lipid infusion. The partitioning theory has been further validated in an in vitro model where the percent decrease in serum drug concentration is proportional to the increase in lipid solubility (21).

The enhanced metabolism theory argues that the infusion of triglycerides and phospholipids provides a sustained fatty acid energy source to myocytes under toxic conditions. Cardiac myocytes preferentially use fatty acids for energy, except in stressed states in which the

Table 1. Xenobiotic Overdose Responses to Intravenous Lipid Emulsion Published in Case Reports and Conference Abstracts from January 2006 to February 2014 Categorized by Class of Drugs and Lipophilicity Drugs (Octanol:Water Partition Coefficient, Log P), Where Values of Log P > 2 are Considered Lipid Soluble

Xenobiotic	Log P*	Positive Effect†	No Apparent Effect†
Lipid soluble (Log P > 2)			
Local anesthetics			
Bupivacaine	3.9	21	
Ropivacaine	2.89	9	2
Lidocaine	2.26	9	1
Cocaine	2.3	2	1
Prilocaine	2.11	1	
Anti-depressant			
Amitriptyline	5.04	9	2
Citalopram	3.63	8	
Bupropion	2.61	5	1
Venlafaxine	3.2	4	
Doxepin	2.4	4	
Dosulepin	2.8	3	
Imipramine	4.8	2	
Escitalopram	3.58‡	2	
Desvenlafaxine	2.6‡	1	
Anti-psychotic			
Quetiapine	3.54	7	2
Olanzapine	3.2	3	
Trazodone	2.52	1	
Acepromazine	2.34	1	
Cardiovascular			
Verapamil	2.31	10	2
Diltiazem	2.7	7	1
Propranolol	3.09	5	2
Amlodipine	3.17	4	2
Propafenone	4.24§	2	
Carvedilol	3.9	2	
Flecainide	3.78	2	
Doxazosin	3.5	1	1
Nebivolol	4.04	1	
Romifidine	2.85‡	1	
Detomidine	2.48‡	1	
Others			
Diphenhydramine	3.4	5	
Zolpidem	2.25	2	
Hydroxychloroquine	3.87‡	1	2
Bromodiolone	6.13‡	1	
Cyclobenzaprine	4.81	1	
Hydroxyzine	4	1	
Endosulfan	3.58	1	
Phenytoin	2.47	1	
Meperidine	2.45	1	
Carbamazepine	2.3	1	
Pentobarbital	2.1	1	
Methamphetamine	2.07	1	
Chloroquine	4.63	0	2
2C-E	3.43	1	
Water soluble (Log P < 2)			
Local anesthetics			
Mepivacaine	1.95	3	1
Cardiovascular			
Metoprolol	1.88	4	1
Atenolol	0.16	2	
Bisoprolol	1.87	1	
Clonidine	1.61	1	
Labetalol	1.24	1	

(Continued)

Table 1. Continued

Xenobiotic	Log P*	Positive Effect†	No Apparent Effect†
Others			
Lamotrigine	1.6	5	1
Baclofen	-0.96	2	
Amphetamine	1.76	1	
Phenobarbital	1.47	1	
Dimenhydrinate	1.1‡	1	
Zopiclone	-0.34	1	
Metformin	-0.31	0	1
Others			
Glyphosate/surfactant	NA	2	
Aconite	NA	1	
Amanita proxima	NA	0	1

NA = Not available.

* Logkow (18).

† Polypharmacy overdoses are counted for each substance in the report likely to contribute the presenting symptoms.

‡ Poulin and Haddad (17).

§ Tetko et al. (19).

myocytes transition to using carbohydrates, a theory that gives credence to the use of high-dose insulin therapy in calcium channel and β -blocker toxicities (24,25). In the development of ILE for local anesthetic toxicity, the hypothesis-generating case was a patient with underlying isovaleria acidemia-induced carnitine deficiency who developed bupivacaine cardiac toxicity at a lower than expected dose (26). In this case, both the carnitine deficiency and bupivacaine, an inhibitor of carnitine transport, likely prevented the carnitine shuttle and subsequent mitochondrial β -oxidation of fatty acids (27). The addition of high-concentration lipids may overwhelm the blockade to allow for fatty acid as an energy source. This theory has since been extrapolated for numerous other cardiotoxic drugs.

Between the two predominant theories, the resolution of both the neurologic and cardiac symptoms of local anesthetic systemic toxicity (LAST) more strongly supports the partition theory. LAST has a spectrum of presentation from cardiovascular collapse to seizures to isolated confusion or hallucinations. Neurons in the central nervous system (CNS) have limited ability to metabolize fatty acids—full restoration of function is difficult to explain by the enhanced metabolism theory. Regardless, the exact mechanism of action has not been fully elucidated and may be a combination of both theories, or an array of other hypotheses yet to be proven.

Lipid Emulsion for Xenobiotic Toxicity

The preponderance of the literature supporting the use of lipid emulsion exists for the management of LAST. Weinberg et al. demonstrated in rat and dog models the rightward shift in the dose–response curve to

bupivacaine-induced cardiotoxicity with the concurrent and resuscitation administration of lipid emulsion therapy (1,2). A subsequent study out of the Weinberg laboratory found superiority in the hemodynamic profile in a rat model of bupivacaine-induced cardiotoxicity with rescue therapy of lipids over both vasopressin and vasopressin with epinephrine (28).

Literature on the use of ILE in humans remains sporadic and is largely limited to case reports. In 2006, Rosenblatt et al. reported the initial case of a successful resuscitation using lipid therapy for intravenous bupivacaine toxicity (3). Subsequent to Dr. Rosenblatt's publication, ILE has been reported to reverse cardiovascular and CNS effects caused by numerous xenobiotics. Approximately 103 cases of lipid therapy have been published through February 2014 (3,16,29–118). Only 16 (15.5%) of the case reports and 6 (15%) of the 40 conference abstracts described "failure" of lipid therapy (4–15). One negative report used ILE in a dosing regimen that was 50 times lower than the recommended dose—making the drug effect difficult to assess (118). Undeniably, both published case reports and unpublished abstracts were biased toward positive effects. Even positive reports must be taken with a grain of salt in the absence of randomized controlled studies. Lipid therapy tends to be one of the last interventions attempted and is usually administered with numerous concurrent therapies. Of the reports demonstrating an apparent treatment benefit, the mean number of therapeutic agents used before lipid therapy was 2.7 and 3.5 for published reports and conference abstracts, respectively. The timing of ILE toward the end of resuscitative efforts places the intervention most proximal to the desired outcome, even though benefits may have resulted from or were synergistic with prior interventions. At times, descriptions of cases where ILE was used for resuscitation contain few details (eg, concomitant use of vasopressors) and ILE may not be included as a keyword, making literature searches difficult.

Table 1 provides a snapshot of the drugs for which lipid emulsion therapy has been used in clinical practice and reported. As mentioned previously, local anesthetic toxicity dominates the literature for the use of ILE, especially bupivacaine, with 21 mentions in either case reports or abstracts. Of note, for all of the reported cases where ILE was used for possible LAST, only two case reports with mixtures of ropivacaine/lidocaine and ropivacaine/mepivacaine suggested that lipid therapy was ineffective (31,117). The most commonly reported nonlocal anesthetics included tricyclic antidepressants (primarily amitriptyline) and verapamil. The great majority of ILE reports were associated with toxicity from lipid-soluble xenobiotics, however, ILE administration is also associated with improvement for poisoning

from numerous water-soluble xenobiotics, such as β -blockers and lamotrigine. The relative efficacy of lipid emulsion therapy for water-soluble xenobiotics compared to lipid-soluble xenobiotics is impossible to comment on, given the paucity and quality of human studies for the therapy. Furthermore, polysubstance ingestions confound the clinical picture of these medications. Some clinical reports used ILE for novel substances (with unknown partition coefficients), such as aconite and glyphosate/surfactant with possible efficacy (12,50,91,119).

Our review of literature identified three prospective studies on the effect of ILE. Minton et al. found minimal blood clearance of amitriptyline and metabolite levels with 500 mL of 20% lipid infusion over 5 h in healthy adult volunteers (120). The results of a randomized controlled trial on the use of ILE in nonlocal anesthetic drug overdose with a heterogeneous overdose population were difficult to interpret (121). Gil et al. found treatment of glyphosate/surfactant overdoses with ILE before symptoms decreased incidence of hypotension and dysrhythmias as compared to historic controls (119). Currently, no prospective randomized controlled trial has been completed to evaluate the efficacy of ILE to reverse toxicity for most of the xenobiotics in Table 1.

Guidelines and Expert Opinions on Use of Lipid Emulsion Rescue

There is no clear consensus on the indications for ILE as a therapy for poisoning. Although the only FDA indications for fat emulsions are essential fatty acid deficiency and total parenteral nutrition, several professional societies have provided guidelines for the use of ILE in a setting of LAST, including the American Society of Regional Anesthesia and Pain Medicine (ASRA) and the Association of Anesthetists of Great Britain and Ireland (122,123). ASRA has published a checklist under the guidance of Dr. Weinberg for the recommended administration of ILE in the management of LAST, which is described here (123). The use of ILE for LAST is also mentioned in the 2010 updates of the American Heart Association guidelines for cardiopulmonary resuscitation in adult and pediatric populations (124,125).

The ACMT interim guideline on lipid resuscitation in therapy in 2011 opines that there is currently no standard of care requirement for the use of lipid emulsion therapy, but that a treating physician may, at his or her discretion, consider the use of this therapy for circumstances of serious hemodynamic instability resultant from lipid-soluble xenobiotics (126). Subsequent to the publication of the ACMT interim guideline statement, a survey of poison center medical directors suggested that 96% and 89% of respondents would administer lipid therapy for cardiac

arrest and shock, respectively, caused by bupivacaine as a single-agent toxicity. Poison centers are less likely to recommend lipid emulsion therapy for verapamil (80% and 62% for cardiac arrest and shock) and amitriptyline (69% and 56% for cardiac arrest and shock) (127).

Administration of Intravenous Lipid Emulsion

The current ILE administration guidelines are extrapolated from recommendations for LAST. Despite 7 years of history with ILE administrations, the recommendations are largely empiric without human trials to substantiate the optimal dose.

Current recommendation from ASRA for 20% lipid emulsion therapy (123):

1. Bolus 1.5 mL/kg (lean body mass) intravenously over 1 min (note, that dose is in volume, not weight)
 - 100 mL for a 70-kg patient
 - Repeat bolus for persistent cardiovascular collapse
2. Continuous infusion 0.25 mL/kg/min
 - 18 mL/min for a 70-kg patient
 - Can double the infusion rate for persistent hemodynamic instability
 - Continue infusion for at least ten minutes after hemodynamic recovery

In the setting of persistent cardiovascular collapse or hemodynamic instability, the upper limits of therapy are also not established. ASRA recommends the upper limits of 10 mL/kg (700 mL in a 70-kg patient) over the first 30 min. Despite the recommendations, actual clinical practice varies greatly among the documented cases, especially for infusion rate and duration of therapy. One case reported the administration of 46 mL/kg (about 4 L) over 12 h in a pediatric patient with only mild adverse effects and successful management of hypotension and seizures in the setting of a bupropion, hydroxyzine, and citalopram overdose (35). Most reports of successful administration of lipid emulsion therapy were within the upper limits of 10 mL/kg total dose.

Regarding pregnancy, ILE has been used successfully as parenteral nutrition without adverse fetal effects. ILE was used to resuscitate an 18-year-old pregnant female at 38 weeks presenting with likely bupivacaine toxicity with good maternal and fetal outcomes (81,128).

Adverse Effects of Lipid Emulsions

Prolonged use of lipid emulsions as parenteral nutrition has been well studied with known risks, however, the novel use of lipid emulsion as a short-term and high-volume resuscitation therapy has limited experience. A total of 19 human case reports document adverse

events that may be attributable to lipid emulsions (35,56,60,68,76,86,87,95,98,99,115). Most prominently lipemic serum was documented in these cases, an obvious finding present after iatrogenic triglyceride administration. In high-enough concentrations, serum triglycerides interfere with routine laboratory analysis. Cases of lipid emulsion administration were associated with “extreme lipemia” that prevented the analysis of serum electrolytes (basic metabolic panel), hematocrit (complete blood count), liver function tests, and coagulation function for hours (up to 39 h) (86,87). Ultracentrifugation was necessary to measure electrolytes 3 h after administration (87). Punja et al. described a false-negative aspartate transaminase attributed to hyperlipidemia that resulted in the premature discontinuation of n-acetylcysteine (76). Similarly, bilirubin analysis in the setting of elevated plasma lipid concentrations can be difficult to measure, but in the acute setting may have limited therapeutic implications.

Levine et al. reported a case of acute pancreatitis and acute respiratory distress syndrome in a 13-year-old female patient who received the ASRA recommended dose of lipid emulsion therapy for a tricyclic antidepressant overdose. Her lipase level peaked at 1849 U/L on day 5 post administration of lipids (60). Serum amylase elevations have also been reported (56,68).

Most recently, Cole et al. published two cases of bupropion/metoprolol and diltiazem/propranolol overdoses where, shortly after ILE administration, both patients had asystolic arrests. Although the relationship is only temporally related, the authors provide cautious reflection on the potential adverse impact of ILE on resuscitation medications and tissue oxygenation, as well as the potential to increase intestinal absorption of offending xenobiotics (16).

Additionally, use lipids with caution in settings of potential relative contraindications, including history of hypersensitivity to lipid emulsion or ingredients (eggs, soy, etc.), severe sepsis, severe liver disease, acute pancreatitis, and acute myocardial infarction (129). No contraindications are absolute in the setting of cardiovascular collapse.

Considerations for Stocking Lipid Emulsions in Emergency Departments

Lipid emulsions, including Intralipid[®], Liposyn[®] III, ClinOleic, and SMOFlipid[™] can be stored at room temperature (< 25°C) in any rapidly accessible location where resuscitation or regional nerve blocks are performed (129–132). Using the ASRA dose recommendations, 500-mL bags of lipid emulsion will likely be sufficient for adult resuscitations. These bags of lipid emulsions may be kept with drug and equipment dispensers,

including crash carts. Wholesale acquisition cost for 12 bags of 500 mL 20% Intralipid® by Baxter Healthcare is listed as \$620.28 or \$51.69 per bag, and 12 bags of 500 mL 20% Liposyn® III by Hospira costs \$213.24 or \$17.77 per bag (133). Additionally, instructional cards with ASRA guidelines can be found and printed from www.lipidrescue.com for quick referencing in resuscitation scenarios.

Toxicology Service Consultation

The decision to administer ILE may be difficult yet at times crucial to the resuscitative efforts of emergency department patients. Local poison centers are available anytime for consultation with specialists in poison information and board-certified medical toxicologists at 1-800-222-1222.

CONCLUSIONS

Since the initial successful report for use in acute bupivacaine-induced cardiac arrest in 2006, intravenous lipid emulsion has been broadly applied for neurologic and cardiac toxic medications. The predominant theory of the lipid sink phenomenon makes this therapy potentially applicable for a wide variety of lipid-soluble xenobiotic-induced toxicities, including local anesthetics, non-dihydropyridine calcium channel blockers, and tricyclic antidepressants. However, the exact mechanism of action has not yet been elucidated and reports of successful resuscitation using lipid emulsion have broadened to include water-soluble xenobiotics, such as β -blockers and lamotrigine. Unfortunately, the lack of high-quality controlled human studies and substantial publication bias toward positive results precludes lipid emulsion therapy as a first-line agent for indications other than local anesthetic systemic toxicity. In the setting of severe hemodynamic compromise caused by a lipid-soluble xenobiotic lipid emulsion therapy may be considered for resuscitation but is not considered to be the standard of care at this time. As such, lipid emulsions may be stocked in emergency departments in close proximity to resuscitation rooms and areas where local nerve blocks are performed. Future larger prospective or registry-based studies may elucidate the true therapeutic effects of ILE in xenobiotic-induced toxicities.

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ARTICLE SUMMARY

1. Why is this topic important?

Intravenous lipid emulsion (ILE) has been broadly applied for neurologic and cardiac toxic medications since initial use as an antidote in an acute bupivacaine-induced cardiac arrest in 2006. The indications for use in the emergency department continue to perplex providers and have been shrouded with uncertainty.

2. What does this review attempt to show?

The review aims to familiarize emergency providers with the indications, availability, dosing recommendations and common adverse reactions associated with ILE use based on a systemic literature search of the human experience with ILE since its inception through January 2014.

3. What are the key findings?

Ninety-four published articles and 40 conference abstracts were identified for review of use of ILE. Most common use for ILE was for local anesthetic toxicity, especially bupivacaine. The most common nonlocal anesthetic xenobiotics for which ILE was used were tricyclic antidepressants and verapamil. No standard of care is defined for the use of ILE. The American Heart Association recommends use in local anesthetic systemic toxicity, and the American College of Medical Toxicology recommends consideration for circumstances of hemodynamic instability resultant from lipid-soluble xenobiotics. Laboratory interference, pancreatitis, respiratory distress syndrome, and interference with vasopressors should be considered as risks.

4. How is patient care impacted?

In the setting of severe hemodynamic compromise caused by a lipid-soluble xenobiotic, lipid emulsion therapy should be considered for resuscitation by emergency physicians, although it is not the standard of care at this time. As such, lipid emulsions may be stocked in emergency departments in close proximity to resuscitation rooms and areas where local nerve blocks are performed.