Title

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AAEM Position Paper

USE OF INTRAVENOUS FAT EMULSION IN THE EMERGENCY DEPARTMENT FOR THE CRITICALLY ILL POISONED PATIENT

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☐ **Abstract—Background: Multiple case reports of using intravenous fat emulsion (IFE) as an antidote for human poisoning from various xenobiotics have been published over the last decade. Given the rapidly evolving field, emergency physicians may be uncertain about the indications, timing, and dose for IFE treatment. Methods: A PubMed literature search was conducted from January 1996 to November 2015 and limited to human studies written in English and articles with relevant keywords. Guideline statements and nonsystematic reviews were excluded. Studies identified then underwent a structured review of their results. Results: There were 986 papers fulfilling the search criteria screened, and 85 appropriate articles were rigorously reviewed in detail. Recommendations were given on indications, timing, and dose of IFE. Most of these were based on case reports and anecdotal experience. Discussion: In critically ill patients with refractory shock or cardiac arrest after a suspected overdose of local anesthetics or selected xenobiotics, IFE may be considered as a potentially beneficial adjunctive treatment. Despite an abundance of reports on the use of IFE on xenobiotics poisoning, the quality of evidence is suboptimal and fraught with reporting bias. Conclusions: IFE may be an effective antidote in poisonings from various xenobiotics. However, further research is needed to determine its optimal circumstances, timing, and dose of use.** © 2016 Elsevier Inc.

☐ **Keywords—intravenous fat emulsion; poisoned patient; review**

Clinical Practice Paper approved by the American Academy of Emergency Medicine Clinical Practice Committee.

INTRODUCTION

The successful use of intravenous fat emulsion (IFE) for the adverse effects associated with local anesthetics has led to its consideration as an antidote for multiple xenobiotics/substances (1–6). Similar to most toxicology research, the evidence is almost completely reliant on animal experiments and human case reports. In addition to lack of definitive efficacy, there is the question of safety. Fat emboli, acute lung injury, cardiac arrest, and deep venous thrombosis have been associated with IFE use. Hypersensitivity, lipemia, pancreatitis, interference with standard medication therapies, and analytical interference with certain laboratory assays are all concerns of unproven clinical significance (7–11).

Our goal is to supply emergency physicians with a practical guideline for the use of IFE in critically poisoned patients, and provide evidence supporting its therapeutic efficacy. Specific focus was given to xenobiotics overdoses that may benefit from administration of IFE, timing of IFE administration, and recommended dose of IFE.

METHODS

A structured review of the medical literature using PubMed was performed and limited to studies published from January 1996 to November 2015. Inclusion criteria were all studies involving human subjects and written in the English language and containing the following keywords: "intravenous" AND ["fat emulsion" OR "lipid

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emulsion" OR "lipid" OR "intralipid"] AND ["resuscitation" OR "poisoning" OR "toxicity" OR "overdose" OR "antidote" OR "rescue"]. References of selected review articles were also screened for potential additional studies (1–6). The abstracts of the articles found in this search were assessed independently by two of the authors, to determine which papers should be pulled for more detailed review based on their suspected relevance to the clinical question. Studies included for the final detailed review were limited to randomized controlled trials, prospective trials, retrospective cohort trials, case series, and case reports in human subjects. General review articles and abstracts presented at conferences were not included for formal review. Cases documented on the Web forum http://www.lipidrescue.org were excluded as they were not peer-reviewed.

Each of the selected articles was subjected to detailed review by at least two of the authors. The level of the evidence was assigned a Grade of Evidence using the definitions as noted in Table 1 and were based on reference focus, specific research design, and methodology. Each of the selected articles was also subjected to detailed review and assigned a Quality Ranking based on a critical assessment with regard to quality of the design and methodology. This includes Design Consideration (e.g., focus, model structure, presence of controls) and Methodology Consideration (actual methodology utilized). The definitions of the Quality Ranking scores are included in Table 2.

Independent review of the articles as well as discussion and joint review by the authors was undertaken to answer the clinical questions. The references were sorted into three categories: supportive, neutral, and opposed. A table was constructed to assign the supportive references to the appropriate location using both the Grade of Evidence and Quality Ranking.

Table 1. The Definitions of the Grades of Evidence of the Articles

Grade A	Randomized clinical trials or meta-analyses (multiple clinical trials) or randomized clinical trials (smaller trials), *directly* addressing the review issue
Grade B	Randomized clinical trials or meta-analyses (multiple clinical trials) or randomized clinical trials (smaller trials), *indirectly* addressing the review issue
Grade C	Prospective, controlled, nonrandomized, cohort studies
Grade D	Retrospective, nonrandomized, cohort or case-control studies
Grade E	Case series, animal/model scientific investigations, theoretical analyses, or case reports
Grade F	Rational conjecture, extrapolations, unreferenced opinion in literature, or common practice

Table 2. The Definitions of the Quality Ranking Scores of the Articles

Ranking	Design Consideration Present	Methodology Consideration Present	Both Considerations Present
Outstanding	Appropriate	Appropriate	Yes, both present
Good	Appropriate	Appropriate	No, either present
Adequate	Adequate with possible bias	Adequate	No, either present
Poor	Limited or biased	Limited	No, either present
Unsatisfactory	Questionable/ none	Questionable/ none	No, either present

Finally, recommendations were made based on the review of the literature and assigned a level of recommendation that is defined in Table 3.

RESULTS

The PubMed search using the method outlined above resulted in 986 unique articles of human studies written in English. Two emergency physicians independently assessed the abstracts of the articles. A total of 85 articles were deemed appropriate to be included in this summary. These articles include: randomized controlled trials (n = 1), retrospective cohort or case-control studies (n = 4), case series/case reports (n = 79), and editorial/rational conjecture (n = 1).

Recommendation 1 – For Which Substances are There Potential Benefits When IFE is Administered?

Whereas the original animal studies and human case reports of IFE were on its use in local anesthetic overdose, IFE has since been shown to be effective in overdose of multiple xenobiotics. Recently a number of case reports have been published on its use in specific pediatric poisonings as well (12–23). Considering most of our knowledge of IFE in human poisonings came from cases reports, and the paucity of double-blinded placebo-controlled studies, limitations exist with regard to its definitive applicability to patients. It is uncertain what the optimal IFE treatment protocol is for all of these substances. There might also be unstudied xenobiotics, which could be effectively treated with IFE.

We focused on those xenobiotics with some published evidence for beneficial effects of IFE (12–87) As a result, we created two categories: 1 – Probable benefit and 2 – Possible benefit. Tables 4 and 5 list the supportive references along with the appropriate classifications

Table 3. Definitions for Recommendations

Level of Recommendation	Criteria for Level of Recommendation	Mandatory Evidence
Class A (Recommended with outstanding evidence)	• Acceptable • Safe • Useful • Established/definitive	• Level A/B grade • Outstanding quality • Robust • All positive
Class B (Acceptable & appropriate with good evidence)	• Acceptable • Safe • Useful • Not yet definitive	• Level A/B grade lacking • Adequate to Good quality • Most evidence positive • No evidence of harm
Class B 1	• Standard approach	• Higher grades of evidence • Consistently positive
Class B 2	• Optional or alternative approach	• Lower grades of evidence • Generally, but not consistently, positive
Class C (Not acceptable or not appropriate)	• Unacceptable • Unsafe • Not useful	• No positive evidence • Evidence of harm
Class Indeterminate (Unknown)	• Minimal to no evidence	• Minimal to no evidence

using both Grade and Quality of Evidence. Additionally, there were seven neutral or opposed references for this clinical question (88–94).

Probable Benefit (12–19,24–45)

All local anesthetics including:

Bupivacaine
Mepivacaine
Ropivacaine
Levobupivacaine
Prilocaine
Lignocaine
Lidocaine

Possible Benefit (20–23,46–87)

Amitriptyline
Amlodipine
Atenolol
Baclofen
Bupropion
Carbamazepine
Carvedilol
Chlorpromazine
Clomipramine
Cocaine
Diltiazem
Diphenhydramine
Dosulepin
Dothiepin
Doxepin
Endosulfan
Felodipine
Flecainide
Glyphosate/Polyoxyethylene amine surfactant
Haloperidol
Hydroxychloroquine
Imipramine
Lamotrigine
Metoprolol
Nebivolol
Nifedipine
Olanzapine
Pentobarbital
Phenobarbital
Propafenone
Propranolol
Quetiapine
Thiopental
Venlafaxine
Verapamil

Recommendation: IFE is probably beneficial in treatment of local anesthetic overdose. Consultation with a medical toxicologist is recommended prior to initiation of overdose treatment from other xenobiotics. Level of recommendation: Class B2.

Recommendation 2 – When Should IFE Be Administered?

The optimal timing of administration of IFE is unclear and has not been studied adequately. The American College of Medical Toxicology (ACMT) recommends that IFE be used for poisoned patients with hemodynamic or other instability not responding to standard resuscitation measures (97). This is consistent with the circumstances of most case reports (12–87). Reports of IFE given for mental status change only in overdosed patients noted little if any difference in outcome in

Table 4. Grade and Quality Table for Use of Intravenous Fat Emulsion in the Emergency Department

(Ref. #)	Article Information	Grade	Quality	Design/Size
1 (24)	Rosenblatt MA, Abel M, Fischer GW, et al. Successful use of a 20% lipid emulsion to resuscitate a patient after a presumed bupivacaine-related cardiac arrest. Anaesthesiology 2006;105:217–8.	E	Poor	Case report (n = 1)
2 (25)	Litz RJ, Popp M, Stehr SN, et al. Successful resuscitation of a patient with ropivacaine-induced asystole after axillary plexus block using lipid infusion. Anaesthesia 2006;61:800–1.	E	Poor	Case report (n = 1)
3 (26)	Spence AG. Lipid reversal of central nervous system symptoms of bupivacaine toxicity. Anaesthesiology 2007;107:516–7.	E	Poor	Case report (n = 1)
4 (27)	Foxall G, McCahon R, Lamb J, et al. Levobupivacaine induced seizures and cardiovascular collapse treated with intralipid. Anaesthesia 2007;62:516–8.	E	Poor	Case report (n = 1)
5 (28)	Litz R, Roessel T, Heller A, et al. Reversal of central nervous system and cardiac toxicity following local anaesthetic intoxication by lipid emulsion injection. Anesth Analg 2008;106:1575–7.	E	Adequate	Case report (n = 1) Drug levels included after IFE given
6 (12)	Ludot H, Tharin J, Belouadah M, et al. Successful resuscitation after ropivacaine and lidocaine induced ventricular arrhythmia following posterior lumbar plexus block in a child. Anaesth Analg 2008;106:1572–4.	E	Adequate	Case report (n = 1) Drug levels included after IFE given
7 (29)	McCutchen T, Gerancher JC. Early intralipid may have prevented bupivacaine associated cardiac arrest. Reg Anaesth Pain Med 2008;33:178–80.	E	Poor	Case report (n = 1)
8 (30)	Smith H, Jacob A, Segura L, et al. Simulation education in anesthesia training: a case report of successful resuscitation of bupivacaine induced cardiac arrest linked to recent simulation training. Anesth Analg 2008;106:1581–4.	E	Poor	Case report (n = 1)
9 (31)	Warren JA, Thoma RB, Georgescu A, et al. Intravenous lipid infusion in the successful resuscitation of local anesthetic induced cardiovascular collapse after supraclavicular brachial plexus block. Anesth Analg 2008;106:1578–80.	E	Adequate	Case report (n = 1) Drug levels included after IFE given
10 (32)	Whiteside J. Reversal of local anaesthetic induced CNS toxicity with lipid emulsion. Anaesthesia 2008;63:203–4.	E	Poor	Case report (n = 1)
11 (33)	Charbonneau H, Marcou TA, Mazoit JX, et al. Early use of lipid emulsion to treat incipient mepivacaine intoxication. Reg Anesth Pain Med 2009;34:277–8.	E	Poor	Case report (n = 1)
12 (34)	Espinet AJ, Emmerton MT. The successful use of intralipid for treatment of local anesthetic induced central nervous system toxicity. Clin J Pain 2009;25:808–9.	E	Poor	Case report (n = 1)
13 (35)	Gnaho A, Eyrieux S, Gentili M. Cardiac arrest during an ultrasound-guided sciatic nerve block combined with nerve stimulation. Reg Anesth Pain Med 2009;34:278.	E	Poor	Case report (n = 1)
14 (13)	Markowitz S, Neal JM. Immediate lipid emulsion therapy in the successful treatment of bupivacaine systemic toxicity. Reg Anesth Pain Med 2009;34:276.	E	Poor	Case report (n = 1)
15 (36)	Marwick PC, Levin AI, Coetzee AR. Recurrence of cardiotoxicity after lipid rescue from bupivacaine induced cardiac arrest. Anesth Analg 2009;108:1344–6.	E	Poor	Case report (n = 1)

(*Continued*)

Table 4. Continued

(Ref. #)	Article Information	Grade	Quality	Design/Size
16 (14)	Shah S, Gopalakrishnan S, Apuya J, et al. Use of Intralipid in an infant with impending cardiovascular collapse due to local anesthetic toxicity. J Anesth 2009;23:439–41.	E	Poor	Case report (n = 1)
17 (37)	Sonsino DH, Fischler M. Immediate intravenous lipid infusion in the successful resuscitation of ropivacaine induced cardiac arrest after infraclavicular brachial plexus block. Reg Anesth Pain Med 2009;34:276–7.	E	Poor	Case report (n = 1)
18 (15)	Cordell CL, Schubkegel T, Light TR, et al. Lipid infusion rescue for bupivicaine-induced cardiac arrest after axillary block. J Hand Surg Am 2010;35:144–6.	E	Poor	Case report (n = 1)
19 (16)	Fuzaylov G, Ying B, Tang Y, et al. Successful resuscitation after inadvertent intravenous injection of bupivacaine in an adolescent. Paediatr Anaesth 2010;20:958–9.	E	Poor	Case report (n = 1)
20 (38)	Gallagher C, Tan JM, Foster CG. Lipid rescue for bupivacaine toxicity during cardiovascular procedures. Heart Int 2010;5:e5	E	Poor	Case report (n = 1)
21 (17)	Lin EP, Aronson LA. Successful resuscitation of bupivacaine-induced cardiotoxicity in a neonate. Paediatr Anaesth 2010;20:955–7.	E	Poor	Case report (n = 1)
22 (18)	Wong GK, Joo DT, McDonnell C. Lipid resuscitation in a carnitine deficient child following intravascular migration of an epidural catheter. Anaesthesia 2010;65:192–5.	E	Adequate	Case report (n = 1) Drug levels included after IFE given
23 (39)	Varela H, Burns SM. Use of lipid emulsions for treatment of local anesthetic toxicity:a case report. AANA J 2010;78:359–64.	E	Poor	Case report (n = 1)
24 (40)	Dix SK, Rosner GF, Nayar M, et al. Intractable cardiac arrest due to lidocaine toxicity successfully resuscitated with lipid emulsion. Crit Care Med 2011;39:872–4.	E	Adequate	Case report (n = 1) Drug levels included after IFE given
25 (41)	Harvey M, Cave G, Chanwai G, et al. Successful resuscitation from bupivacaine-induced cardiovascular collapse with intravenous lipid emulsion following femoral nerve block in an emergency department. Emerg Med Australas 2011;23:209–14.	E	Adequate	Case report (n = 1) Drug levels included after IFE given
26 (42)	Mizutani K, Oda Y, Sato H. Successful treatment of ropivacaine-induced central nervous system toxicity by use of lipid emulsion: effect on total and unbound plasma fractions. J Anesth 2011;25:442–5.	E	Adequate	Case report (n = 1) Drug levels included after IFE given
27 (43)	Shih YH, Chen CH, Wang YM, et al. Successful reversal of bupivacaine and lidocaine-induced severe junctional bradycardia by lipid emulsion following infraclavicular brachial plexus block in a uremic patient. Acta Anaesthesiol Taiwan 2011;49:72–4.	E	Poor	Case report (n = 1)
28 (44)	Lange DB, Schwartz D, DaRoza G, et al. Use of intravenous lipid emulsion to reverse central nervous system toxicity of an iatrogenic local anesthetic overdose in a patient on peritoneal dialysis. Ann Pharmacother 2012;46:e37.	E	Poor	Case report (n = 1)
29 (45)	Nguyen VH, White JL. Further support for the early administration of lipid emulsion in the treatment of ropivacaine-induced central nervous system toxicity. J Anesth 2012;26:479–80.	E	Poor	Case report (n = 1)
30 (19)	Shenoy U, Paul J, Antony D. Lipid resuscitation in pediatric patients – need for caution? Paediatr Anaesth 2014;24:332–4.	E	Poor	Case report (n = 1)

(*Continued*)

Table 4. Continued

(Ref. #)	Article Information	Grade	Quality	Design/Size
31 (20)	Sirianni AJ, Osterhoudt KC, Calello DP, et al. Use of Intralipid in the resuscitation of a patient with prolonged cardiovascular collapse after overdose of bupropion and lamotrigine. Ann Emerg Med 2008;51:412–5.	E	Adequate	Case report (n = 1) Drug levels included prior to IFE given
32 (46)	Finn SD, Uncles DR, Willers J, et al. Early treatment of a quetiapine and sertraline overdose with intralipid. Anaesthesia 2009;64:191–4.	E	Poor	Case report (n = 1)
33 (47)	Weinberg G, Di Gregorio G, Hiller D, et al. Reversal of haloperidol-induced cardiac arrest by using lipid emulsion. Ann Int Med 2009;150:737–8.	E	Poor	Case report (n = 1)
34 (48)	Young AC, Velez LI, Kleinschmidt KC. Intravenous fat emulsion therapy for intentional sustained-release verapamil overdose. Resuscitation 2009;80:591–3.	E	Adequate	Case report (n = 1) Drug levels included prior to IFE given
35 (49)	Dean P, Ruddy JP, Marshall S. Intravenous lipid emulsion in propranolol overdose. Anaesthesia 2010;65:1148–50.	E	Poor	Case report (n = 1)
36 (50)	Engels PT, Davidow JS. Intravenous fat emulsion to reverse haemodynamic instability from intentional amitriptyline overdose. Resuscitation 2010;81:1037–9.	E	Poor	Case report (n = 1)
37 (51)	Han SK, Jeong J, Yeom S, et al. Use of lipid emulsion in a patient with refractory hypotension caused by glyphosate-surfactant herbicide. Clin Toxicol 2010;48:566–8.	E	Poor	Case report (n = 1)
38 (52)	Hillyard SG, Barrera-Groba C, Tighe R. Intralipid reverses coma associated with zopiclone and venlafaxine overdose. Eur J Anaesthiol 2010;27:582–3.	E	Poor	Case report (n = 1)
39 (53)	Stellpflug SJ, Harris CR, Engerbretsen KM, et al. Intentional overdose with cardiac arrest treated with intravenous fat emulsion and high-dose insulin. Clin Toxicol 2010;48:227–9.	E	Poor	Case report (n = 1)
40 (54)	Boegevig S, Rothe A, Tfelt-Hansen J, et al. Successful reversal of life threatening cardiac effect following dosulepin overdose using intravenous lipid emulsion. Clin Toxicol (Phila) 2011;49:337–9.	E	Poor	Case report (n = 1)
41 (55)	Dagtekin O, Marcus H, Müller C, et al. Lipid therapy for serotonin syndrome after intoxication with venlafaxine, lamotrigine and diazepam. Minerva Anestesiol 2011;77:93–5.	E	Adequate	Case report (n = 1) Drug levels included prior to IFE given
42 (56)	Franxman TJ, Al-Nabhan M, Cavallazzi RS, et al. Lipid emulsion therapy for verapamil overdose. Ann Intern Med 2011;154:292.	E	Poor	Case report (n = 1)
43 (57)	French D, Armenian P, Ruan W, et al. Serum verapamil concentrations before and after Intralipid® therapy during treatment of an overdose. Clin Toxicol (Phila) 2011;49:340–4.	E	Good	Case report (n = 1) Drug levels included prior to and after IFE given
44 (58)	Jakkala-Saibaba R, Morgan PG, Morton GL. Treatment of cocaine overdose with lipid emulsion. Anaesthesia 2011;66:1168–70.	E	Poor	Case report (n = 1)
45 (59)	Jovic-Stosic J, Gligic B, Putic V, et al. Severe propranolol and ethanol overdose with wide complex tachycardia treated with intravenous lipid emulsion: a case report. Clin Toxicol (Phila) 2011;49:426–30.	E	Adequate	Case report (n = 1) Drug levels included prior to and after IFE given
46 (21)	Hendron D, Menagh G, Sandilands EA, et al. Tricyclic antidepressant overdose in a toddler treated with intravenous lipid emulsion. Pediatrics 2011;128:e1628–32.	E	Poor	Case report (n = 1)

(*Continued*)

Table 4. Continued

(Ref. #)	Article Information	Grade	Quality	Design/Size
47 (60)	Jacob J, Heard K. Second case of the use of intravenous fat emulsion therapy for propafenone toxicity. Clin Toxicol (Phila) 2011;49:946–7.	E	Poor	Case report (n = 1)
48 (61)	Livshits Z, Feng Q, Chowdhury F, et al. Life-threatening bupropion ingestion: is there a role for intravenous fat emulsion? Basic Clin Pharmacol Toxicol 2011;109:418–22.	E	Adequate	Case report (n = 1) Drug levels included prior to and after IFE given
49 (62)	Montiel V, Gougnard T, Hanston P. Diltiazem poisoning treated with hyperinsulinemic euglycemia therapy and intravenous lipid emulsion. Eur J Emerg Med 2011;18:121–3.	E	Adequate	Case report (n = 1) Drug levels included prior to IFE given
50 (63)	Moussot PE, Marhar F, Minville V, et al. Use of intravenous lipid 20% emulsion for the treatment of a voluntary intoxication of flecainide with refractory shock. Clin Toxicol (Phila) 2011 Jul;49(6):514.	E	Poor	Case report (n = 1)
51 (64)	Stellpflug SJ, Fritzlar SJ, Cole JB, et al. Cardiotoxic overdose treated with intravenous fat emulsion and high-dose insulin in the setting of hypertrophic cardiomyopathy. J Med Toxicol 2011;7:151–3.	E	Adequate	Case report (n = 1) Drug levels included prior to IFE given
52 (65)	ten Tusscher BL, Beishuizen A, Girbes AR, et al. Intravenous fat emulsion therapy for intentional propafenone intoxication. Clin Toxicol (Phila) 2011;49(7):701.	E	Poor	Case report (n = 1)
53 (66)	Blaber MS, Khan JN, Brebner JA, et al. "Lipid rescue" for tricyclic antidepressant cardiotoxicity. J Emerg Med 2012;43:465–7.	E	Poor	Case report (n = 1)
54 (67)	Castanares-Zapatero D, Wittebole X, Huberlant V, et al. Lipid emulsion as rescue therapy in lamotrigine overdose. J Emerg Med 2012;42:48–51.	E	Adequate	Case report (n = 1) Drug levels included prior to IFE given
55 (68)	Geib AJ, Liebelt E, Manini AF;Toxicology Investigators' Consortium (ToxIC). Clinical experience with intravenous lipid emulsion for drug-induced cardiovascular collapse. J Med Toxicol 2012;8:10–4.	D	Good	Retrospective review (n = 9)
56 (69)	Haesendonck R, de Winter S, Verelst S, et al. Intravenous lipid emulsion for intentional Chloroquine poisoning. Clin Toxicol (Phila) 2012;50:223.	E	Poor	Case report (n = 1)
57 (22)	Levine M, Brooks DE, Franken A, et al. Delayed-onset seizure and cardiac arrest after amitriptyline overdose, treated with intravenous lipid emulsion therapy. Pediatrics 2012;130:e432–8.	E	Adequate	Case report (n = 1) Drug levels included prior to and after IFE given
58 (23)	McAllister RK, Tutt CD, Colvin CS. Lipid 20% emulsion ameliorates the symptoms of olanzapine toxicity in a 4-year-old. Am J Emerg Med 2012;30: 1012e1–2.	E	Poor	Case report (n = 1)
59 (70)	Taftachi F, Sanaei-Zadeh H, Sepehrian B, et al. Lipid emulsion improves Glasgow coma scale and decreases blood glucose level in the setting of acute non-local anesthetic drug poisoning—a randomized controlled trial. Eur Rev Med Pharmacol Sci 2012;16(Suppl 1):38–42.	B	Good	Randomized controlled trial (n = 30)
60 (71)	Wilson BJ, Cruikshank JS, Wiebe KL, et al. Intravenous lipid emulsion therapy for sustained release diltiazem poisoning: a case report. J Popul Ther Clin Pharmacol 2012;19:e218–22.	E	Adequate	Case report (n = 1) Drug levels included prior to and after IFE given

(*Continued*)

Table 4. Continued

(Ref. #)	Article Information	Grade	Quality	Design/Size
61 (72)	You Y, Jung WJ, Lee MJ. Effect of intravenous fat emulsion therapy on glyphosate-surfactant-induced cardiovascular collapse. Am J Emerg Med 2012;30:2097.e1–2.	E	Poor	Case report (n = 1)
62 (73)	Yurtlu BS, Hanci V, Gür A, et al. Intravenous lipid infusion restores consciousness associated with olanzapine overdose. Anesth Analg 2012;114:914–5.	E	Poor	Case report (n = 1)
63 (74)	Arora NP, Berk WA, Aaron CK, et al. Usefulness of intravenous lipid emulsion for cardiac toxicity from cocaine overdose. Am J Cardiol 2013;111:445–7.	E	Poor	Case report (n = 1)
64 (75)	Arslan ED, Demir A, Yilmaz F, et al. Treatment of quetiapine overdose with intravenous lipid emulsion. Keio J Med 2013;62:53–7.	E	Poor	Case report (n = 1)
65 (76)	Bartos M, Knudsen K. Use of intravenous lipid emulsion in the resuscitation of a patient with cardiovascular collapse after a severe overdose of quetiapine. Clin Toxicol (Phila) 2013;51:501–4.	E	Adequate	Case report (n = 1) Drug levels included prior to and after IFE given
66 (77)	Bologa C, Lionte C, Coman A, et al. Lipid emulsion therapy in cardiodepressive syndrome after diltiazem overdose–case report. Am J Emerg Med 2013;31:1154.e3–4.	E	Poor	Case report (n = 1)
67 (78)	Ellsworth H, Stellpflug SJ, Cole JB, et al. A life-threatening flecainide overdose treated with intravenous fat emulsion. Pacing Clin Electrophysiol 2013;36:e87–9.	E	Adequate	Case report (n = 1) Drug levels included prior to and after IFE given
68 (79)	Gil HW, Park JS, Park SH, et al. Effect of intravenous lipid emulsion in patients with acute glyphosate intoxication. Clin Toxicol (Phila) 2013;51:767–71.	D	Good	Case-control study (n = 44)
69 (80)	Moon HJ, Lee JW. Availability of intravenous lipid emulsion therapy on endosulfan-induced cardiovascular collapse. Am J Emerg Med 2013;31:886.e1–2.	E	Poor	Case report (n = 1)
70 (81)	Sivalingam SK, Gadiraju VT, Hariharan MV, et al. Flecainide toxicity—treatment with intravenous fat emulsion and extra corporeal life support. Acute Card Care 2013;15:90–2.	E	Adequate	Case report (n = 1) Drug levels included prior to IFE given
71 (82)	Abdi A, Rose E, Levine M. Diphenhydramine overdose with intraventricular conduction delay treated with hypertonic sodium bicarbonate and i.v. lipid emulsion. West J Emerg Med 2014;15:855–8.	E	Adequate	Case report (n = 1) Drug levels included prior to IFE given
72 (83)	Abdelmalek D, Schwarz ES, Sampson C, et al. Life-threatening diphenhydramine toxicity presenting with seizures and a wide complex tachycardia improved with intravenous fat emulsion. Am J Ther 2014;21:542–4.	E	Adequate	Case report (n = 1) Drug levels included prior to IFE given
73 (84)	Agarwala R, Ahmed SZ, Wiegand TJ. Prolonged use of intravenous lipid emulsion in a severe tricyclic antidepressant overdose. J Med Toxicol 2014;10:210–4.	E	Adequate	Case report (n = 1) Drug levels included prior to and after IFE given
74 (85)	Doepker B, Healy W, Cortez E, et al. High-dose insulin and intravenous lipid emulsion therapy for cardiogenic shock induced by intentional calcium-channel blocker and Beta-blocker overdose: a case series. J Emerg Med 2014;46:486–90.	E	Poor	Case series (n = 2)
75 (86)	Eren Cevik S, Tasyurek T, Guneysel O. Intralipid emulsion treatment as an antidote in lipophilic drug intoxications. Am J Emerg Med 2014;32:1103–8.	E	Poor	Case series (n = 10)

(*Continued*)

Table 4. Continued

(Ref. #)	Article Information	Grade	Quality	Design/Size
76 (87)	Sebe A, Dişel NR, Açıkalın Akpınar A, et al. Role of intravenous lipid emulsions in the management of calcium channel blocker and β-blocker overdose: 3 years experience of a university hospital. Postgrad Med 2015;127:119–24.	D	Adequate	Retrospective study (n = 15)
77 (88)	Calenda E, Dinescu SA. Failure of lipid emulsion to reverse neurotoxicity after an ultrasound-guided axillary block with ropivacaine and mepivacaine. J Anesth 2009;23:472–3.	E	Poor	Case report (n = 1)
78 (89)	Watt P, Malik D, Dyson L. Gift of the glob—is it foolproof? Anaesthesia 2009;64:1031–3.	E	Poor	Case series (n = 2)
79 (90)	West PL, McKeown NJ, Hendrickson RG. Iatrogenic lipid emulsion overdose in a case of amlodipine poisoning. Clin Toxicol (Phila) 2010;48: 293–6.	E	Adequate	Case report (n = 1) Drug levels included after IFE given
80 (91)	Kiberd MB, Minor SF. Lipid therapy for the treatment of a refractory amitriptyline overdose. CJEM 2012;14:193–7.	E	Poor	Case report (n = 1)
81 (92)	Kundu R, Almasri H, Moza A, et al. Intravenous lipid emulsion in wide complex arrhythmia with alternating bundle branch block pattern from cocaine overdose. Kardiol Pol 2013;71:1073–5.	E	Poor	Case report (n = 1)
82 (93)	Bazerbachi F, Rank K, Chan A. Intravenous lipid rescue and ropivacaine systemic toxicity. J Anesth 2014;28:139.	E	Poor	Case report (n = 1)
83 (94)	Downes MA, Calver LA, Isbister GK. Intralipid therapy does not improve level of consciousness in overdoses with sedating drugs: a case series. Emerg Med Australas 2014;26:286–90.	D	Adequate	Retrospective chart review (n = 9)
84 (95)	Rodríguez B, Wilhelm A, Kokko KE. Lipid emulsion use precluding renal replacement therapy. J Emerg Med 2014;47:635–7.	E	Poor	Case report (n = 1)
85 (96)	Fettiplace MR, Akpa BS, Rubinstein I, et al. Confusion about Infusion: rational volume limits for intravenous lipid emulsion during treatment of oral overdoses. Ann Emerg Med 2015;66:185–8.	F	Poor	Rational conjecture/Editorial

IFE = intravenous fat emulsion.

some cases, but clinically significant improvement in others (70,73,89,94). Furthermore, IFE has not been directly compared with (and proven to be more effective than) standard seizure therapies such as benzodiazepines.

Table 5. Evidence Rating (Article# Referenced in Table 4)

Quality/Grade	A	B	C	D	E	F
Outstanding						
Good		59		55,68	43	
Adequate				76,83	5,6,9,22,24–26, 31,34,41,45, 48, 49,51,54,57,60, 65,67,70–73,79	
Poor					1–4,7,8,10–21,23, 27–30,32,33, 35–40,42,44,46,47,50,52, 53,56,58,61–64, 66,69,74,75,77,78, 80–82,84	85
Unsatisfactory						

It is therefore reasonable to recommend that IFE be given in patients overdosed on local anesthetics who show signs of cardiovascular collapse or refractory shock. This should be done concomitantly with standard cardiopulmonary resuscitation according to the Advanced Cardiac Life Support protocol, inotropes and pressors administration. Similarly, IFE should be considered for overdose of other xenobiotics (see list under recommendation 1) in cases of cardiac arrest or refractory shock where standard resuscitation therapies have failed or would not be considered efficacious.

Recommendation: IFE is recommended in conjunction with standard resuscitation therapies in poisoned patients who are hemodynamically unstable. Level of recommendation: Class B2.

Recommendation 3 – What Dose and Duration of IFE Should Be Used?

Twenty percent IFE has been the most commonly studied formulation in poisonings, though other lipid formulations exist with varying concentrations. The ACMT recommends that 20% IFE be given as a 1.5-mL/kg bolus, which may be repeated in cases of asystole or pulseless electrical activity. This may be followed by an infusion of 0.25 mL/kg/min for up to 60 min. In case of re-emergence of hemodynamic instability after initial response, the bolus could be repeated or the infusion rate could be increased (97). The Association of Anaesthetists of Great Britain and Ireland guidelines recommends a similar regimen with a maximum dose of 12 mL/kg for local anesthetic toxicity (98).

These recommendations were derived from cases of local anesthetic poisoning, which tend to be short lived. In addition, the maximal duration of IFE infusion was not specified. The United States Food and Drug Administration recommends an upper limit of 12.5 mL/kg of 20% IFE over 24 h in adults, and 15 mL/kg over 24 h in pediatric patients, though this was established with the intention of IFE being used as a nutritional infusion rather than an antidote. In practice, when IFE was used for nonlocal anesthetic poisoning, infusion of up to 19 days, and total volume as high as 6200 mL (79 mL/kg body weight), over 5 h have been reported (84,95).

In a recent article, Fettiplace et al. recommended a maximum initial 20% IFE load of 2.25 mL/kg, followed by 0.025 mL/kg/min if needed, for no more than 6.5 hours, as a balance between benefits and potential adverse effects (96). This would ideally need to be validated by future clinical trials.

Recommendation: Twenty percent IFE can be given as a 1.5-mL/kg bolus in case of xenobiotics poisoning. Consider repeat dose(s) every 5 min until cardiovascular stability is achieved. This may be followed by an infusion of 0.025–0.25 mL/kg/min. Preferably, total 24 h dosing should be under 12.5 mL/kg. Level of recommendation: Class B2.

DISCUSSION

In this article, we have reviewed the current published literature and made recommendations of the indications, timing, and dose of IFE use in cases of xenobiotics poisoning. In critically ill patients with refractory shock or cardiac arrest after a suspected overdose of local anesthetic and other listed agents, IFE may be considered as a potentially beneficial adjunctive treatment. A bolus dose of 1.5 mL/kg seems reasonable, which may be repeated and followed by an infusion of 0.025–0.25 mL/kg/min if needed. Early consultation with a medical toxicologist should be considered to guide the exact course of therapy.

Reporting bias limits the definitive interpretation of the existing literature. In addition, human evidence is limited to mostly case reports that provide most of our current knowledge beyond animal studies regarding the efficacy of IFE. IFE deserves more rigorous human studies. International databases such as those of the Toxicology Investigators Consortium (ToxIC) show promise to provide more answers in the future (68).

CONCLUSION

In critically ill patients with a suspected overdose of local anesthetics, IFE should be considered as a potentially beneficial adjunctive treatment. For overdose of all other xenobiotics, consultation with a medical toxicologist may be warranted to determine risk vs. benefit. Studies with more rigorous designs are needed to elaborate on its optimal indications, timing, and dose.

REFERENCES

1. Cave G, Harvey M, Graudins A. Intravenous lipid emulsion as antidote: a summary of published human experience. Emerg Med Australas 2011;23:123–41.
2. Waring WS. Intravenous lipid administration for drug-induced toxicity: a critical review of the existing data. Expert Rev Clin Pharmacol 2012;5:437–44.
3. Jamaty C, Bailey B, Larocque A, et al. Lipid emulsions in the treatment of acute poisoning: a systematic review of human and animal studies. Clin Toxicol (Phila) 2010;48:1–27.
4. Weinberg GL. Lipid emulsion infusion: resuscitation for local anesthetic and other drug overdose. Anesthesiology 2012;117:180–7.
5. Cave G, Harvey M. Intravenous lipid emulsion as antidote beyond local anesthetic toxicity: a systematic review. Acad Emerg Med 2009;16:815–24.
6. Presley JD, Chyka PA. Intravenous lipid emulsion to reverse acute drug toxicity in pediatric patients. Ann Pharmacother 2013;47:735–43.
7. Bucklin MH, Gorodetsky RM, Wiegand TJ. Prolonged lipemia and pancreatitis due to extended infusion of lipid emulsion in bupropion overdose. Clin Toxicol (Phila) 2013;51:896–8.
8. Cole JB, Stellpflug SJ, Engebretsen KM. Asystole immediately following intravenous fat emulsion for overdose. J Med Toxicol 2014;10:307–10.
9. Levine M, Skolnik AB, Ruha AM, et al. Complications following antidotal use of intravenous lipid emulsion therapy. J Med Toxicol 2014;10:10–4.
10. Martin C, Gonzalez H, Ruiz S, et al. Acute respiratory distress syndrome following verapamil overdose treated with intravenous lipid emulsion: a rare life-threatening complication. Ann Fr Anesth Reanim 2014;33:e101–2.
11. Grunbaum AM, Gilfix BM, Gosselin S, Blank DW. Analytical interferences resulting from intravenous lipid emulsion. Clin Toxicol (Phila) 2012;50:812–7.
12. Ludot H, Tharin J, Belouadah M, et al. Successful resuscitation after ropivacaine and lidocaine induced ventricular arrhythmia following posterior lumbar plexus block in a child. Anaesth Analg 2008;106:1572–4.
13. Markowitz S, Neal JM. Immediate lipid emulsion therapy in the successful treatment of bupivacaine systemic toxicity. Reg Anesth Pain Med 2009;34:276.

14. Shah S, Gopalakrishnan S, Apuya J, et al. Use of Intralipid in an infant with impending cardiovascular collapse due to local anesthetic toxicity. J Anesth 2009;23:439–41.
15. Cordell CL, Schubkegel T, Light TR, et al. Lipid infusion rescue for bupivicaine-induced cardiac arrest after axillary block. J Hand Surg Am 2010;35:144–6.
16. Fuzaylov G, Ying B, Tang Y, et al. Successful resuscitation after inadvertent intravenous injection of bupivacaine in an adolescent. Paediatr Anaesth 2010;20:958–9.
17. Lin EP, Aronson LA. Successful resuscitation of bupivacaine-induced cardiotoxicity in a neonate. Paediatr Anaesth 2010;20:955–7.
18. Wong GK, Joo DT, McDonnell C. Lipid resuscitation in a carnitine deficient child following intravascular migration of an epidural catheter. Anaesthesia 2010;65:192–5.
19. Shenoy U, Paul J, Antony D. Lipid resuscitation in pediatric patients - need for caution? Paediatr Anaesth 2014;24:332–4.
20. Sirianni AJ, Osterhoudt KC, Calello DP, et al. Use of Intralipid in the resuscitation of a patient with prolonged cardiovascular collapse after overdose of bupropion and lamotrigine. Ann Emerg Med 2008; 51:412–5.
21. Hendron D, Menagh G, Sandilands EA, et al. Tricyclic antidepressant overdose in a toddler treated with intravenous lipid emulsion. Pediatrics 2011;128:e1628–32.
22. Levine M, Brooks DE, Franken A, et al. Delayed-onset seizure and cardiac arrest after amitriptyline overdose, treated with intravenous lipid emulsion therapy. Pediatrics 2012;130:e432–8.
23. McAllister RK, Tutt CD, Colvin CS. Lipid 20% emulsion ameliorates the symptoms of olanzapine toxicity in a 4-year-old. Am J Emerg Med 2012;30:1012e1–2.
24. Rosenblatt MA, Abel M, Fischer GW, et al. Successful use of a 20% lipid emulsion to resuscitate a patient after a presumed bupivacaine-related cardiac arrest. Anaestheiology 2006;105:217–8.
25. Litz RJ, Popp M, Stehr SN, et al. Successful resuscitation of a patient with ropivacaine-induced asystole after axillary plexus block using lipid infusion. Anaesthesia 2006;61:800–1.
26. Spence AG. Lipid reversal of central nervous system symptoms of bupivacaine toxicity. Anaesthesiology 2007;107:516–7.
27. Foxall G, McCahon R, Lamb J, et al. Levobupivacaine induced seizures and cardiovascular collapse treated with intralipid. Anaesthesia 2007;62:516–8.
28. Litz R, Roessel T, Heller A, et al. Reversal of central nervous system and cardiac toxicity following local anaesthetic intoxication by lipid emulsion injection. Anesth Analg 2008;106:1575–7.
29. McCutchen T, Gerancher JC. Early intralipid may have prevented bupivacaine associated cardiac arrest. Reg Anaesth Pain Med 2008;33:178–80.
30. Smith H, Jacob A, Segura L, et al. Simulation education in anesthesia training: a case report of successful resuscitation of bupivacaine induced cardiac arrest linked to recent simulation training. Anesth Analg 2008;106:1581–4.
31. Warren JA, Thoma RB, Georgescu A, et al. Intravenous lipid infusion in the successful resuscitation of local anesthetic induced cardiovascular collapse after supraclavicular brachial plexus block. Anesth Analg 2008;106:1578–80.
32. Whiteside J. Reversal of local anaesthetic induced CNS toxicity with lipid emulsion. Anaesthesia 2008;63:203–4.
33. Charbonneau H, Marcou T, Mazoit JX, et al. Early use of lipid emulsion to treat incipient mepivacaine intoxication. Reg Anesth Pain Med 2009;34:277–8.
34. Espinet AJ, Emmerton MT. The successful use of intralipid for treatment of local anesthetic induced central nervous system toxicity. Clin J Pain 2009;25:808–9.
35. Gnaho A, Eyrieux S, Gentili M. Cardiac arrest during an ultrasound-guided sciatic nerve block combined with nerve stimulation. Reg Anesth Pain Med 2009;34:278.
36. Marwick PC, Levin AI, Coetzee AR. Recurrence of cardiotoxicity after lipid rescue from bupivacaine induced cardiac arrest. Anesth Analg 2009;108:1344–6.
37. Sonsino DH, Fischler M. Immediate intravenous lipid infusion in the successful resuscitation of ropivacaine induced cardiac arrest after infraclavicular brachial plexus block. Reg Anesth Pain Med 2009;34:276–7.
38. Gallagher C, Tan JM, Foster CG. Lipid rescue for bupivacaine toxicity during cardiovascular procedures. Heart Int 2010;5:e5.
39. Varela H, Burns SM. Use of lipid emulsions for treatment of local anesthetic toxicity: a case report. AANA J 2010;78:359–64.
40. Dix SK, Rosner GF, Nayar M, et al. Intractable cardiac arrest due to lidocaine toxicity successfully resuscitated with lipid emulsion. Crit Care Med 2011;39:872–4.
41. Harvey M, Cave G, Chanwai G, et al. Successful resuscitation from bupivacaine-induced cardiovascular collapse with intravenous lipid emulsion following femoral nerve block in an emergency department. Emerg Med Australas 2011;23:209–14.
42. Mizutani K, Oda Y, Sato H. Successful treatment of ropivacaine-induced central nervous system toxicity by use of lipid emulsion: effect on total and unbound plasma fractions. J Anesth 2011;25: 442–5.
43. Shih YH, Chen CH, Wang YM, et al. Successful reversal of bupivacaine and lidocaine-induced severe junctional bradycardia by lipid emulsion following infraclavicular brachial plexus block in a uremic patient. Acta Anaesthesiol Taiwan 2011;49:72–4.
44. Lange DB, Schwartz D, DaRoza G, et al. Use of intravenous lipid emulsion to reverse central nervous system toxicity of an iatrogenic local anesthetic overdose in a patient on peritoneal dialysis. Ann Pharmacother 2012;46:e37.
45. Nguyen VH, White JL. Further support for the early administration of lipid emulsion in the treatment of ropivacaine-induced central nervous system toxicity. J Anesth 2012;26:479–80.
46. Finn SD, Uncles DR, Willers J, et al. Early treatment of a quetiapine and sertraline overdose with intralipid. Anaesthesia 2009;64:191–4.
47. Weinberg G, Di Gregorio G, Hiller D, et al. Reversal of haloperidol-induced cardiac arrest by using lipid emulsion. Ann Int Med 2009; 150:737–8.
48. Young AC, Velez LI, Kleinschmidt KC. Intravenous fat emulsion therapy for intentional sustained-release verapamil overdose. Resuscitation 2009;80:591–3.
49. Dean P, Ruddy JP, Marshall S. Intravenous lipid emulsion in propranolol overdose. Anaesthesia 2010;65:1148–50.
50. Engels PT, Davidow JS. Intravenous fat emulsion to reverse haemodynamic instability from intentional amitriptyline overdose. Resuscitation 2010;81:1037–9.
51. Han SK, Jeong J, Yeom S, et al. Use of lipid emulsion in a patient with refractory hypotension caused by glyphosate-surfactant herbicide. Clin Toxicol 2010;48:566–8.
52. Hillyard SG, Barrera-Groba C, Tighe R. Intralipid reverses coma associated with zopiclone and venlafaxine overdose. Eur J Anaesthiol 2010;27:582–3.
53. Stellpflug SJ, Harris CR, Engerbretsen KM, et al. Intentional overdose with cardiac arrest treated with intravenous fat emulsion and high-dose insulin. Clin Toxicol (Phila) 2010;48:227–9.
54. Boegevig S, Rothe A, Tfelt-Hansen J, et al. Successful reversal of life threatening cardiac effect following dosulepin overdose using intravenous lipid emulsion. Clin Toxicol (Phila) 2011;49:337–9.
55. Dagtekin O, Marcus H, Müller C, et al. Lipid therapy for serotonin syndrome after intoxication with venlafaxine, lamotrigine and diazepam. Minerva Anestesiol 2011;77:93–5.
56. Franxman TJ, Al-Nabhan M, Cavallazzi RS, et al. Lipid emulsion therapy for verapamil overdose. Ann Intern Med 2011;154:292.
57. French D, Armenian P, Ruan W, et al. Serum verapamil concentrations before and after Intralipid® therapy during treatment of an overdose. Clin Toxicol (Phila) 2011;49:340–4.
58. Jakkala-Saibaba R, Morgan PG, Morton GL. Treatment of cocaine overdose with lipid emulsion. Anaesthesia 2011;66:1168–70.
59. Jovic-Stosic J, Gligic B, Putic V, et al. Severe propranolol and ethanol overdose with wide complex tachycardia treated with intravenous lipid emulsion: a case report. Clin Toxicol (Phila) 2011;49: 426–30.
60. Jacob J, Heard K. Second case of the use of intravenous fat emulsion therapy for propafenone toxicity. Clin Toxicol (Phila) 2011; 49:946–7.

61. Livshits Z, Feng Q, Chowdhury F, et al. Life-threatening bupropion ingestion: is there a role for intravenous fat emulsion? Basic Clin Pharmacol Toxicol 2011;109:418–22.
62. Montiel V, Gougnard T, Hanston P. Diltiazem poisoning treated with hyperinsulinemic euglycemia therapy and intravenous lipid emulsion. Eur J Emerg Med 2011;18:121–3.
63. Moussot PE, Marhar F, Minville V, et al. Use of intravenous lipid 20% emulsion for the treatment of a voluntary intoxication of flecainide with refractory shock. Clin Toxicol (Phila) 2011;49:514.
64. Stellpflug SJ, Fritzlar SJ, Cole JB, et al. Cardiotoxic overdose treated with intravenous fat emulsion and high-dose insulin in the setting of hypertrophic cardiomyopathy. J Med Toxicol 2011;7:151–3.
65. ten Tusscher BL, Beishuizen A, Girbes AR, et al. Intravenous fat emulsion therapy for intentional propafenone intoxication. Clin Toxicol (Phila) 2011;49:701.
66. Blaber MS, Khan JN, Brebner JA, et al. "Lipid rescue" for tricyclic antidepressant cardiotoxicity. J Emerg Med 2012;43:465–7.
67. Castanares-Zapatero D, Wittebole X, Huberlant V, et al. Lipid emulsion as rescue therapy in lamotrigine overdose. J Emerg Med 2012;42:48–51.
68. Geib AJ, Liebelt E, Manini AF, Toxicology Investigators' Consortium (ToxIC). Clinical experience with intravenous lipid emulsion for drug-induced cardiovascular collapse. J Med Toxicol 2012;8:10–4.
69. Haesendonck R, de Winter S, Verelst S, et al. Intravenous lipid emulsion for intentional Chloroquine poisoning. Clin Toxicol (Phila) 2012;50:223.
70. Taftachi F, Sanaei-Zadeh H, Sepehrian B, et al. Lipid emulsion improves Glasgow coma scale and decreases blood glucose level in the setting of acute non-local anesthetic drug poisoning–a randomized controlled trial. Eur Rev Med Pharmacol Sci 2012;16(Suppl 1):38–42.
71. Wilson BJ, Cruikshank JS, Wiebe KL, et al. Intravenous lipid emulsion therapy for sustained release diltiazem poisoning: a case report. J Popul Ther Clin Pharmacol 2012;19:e218–22.
72. You Y, Jung WJ, Lee MJ. Effect of intravenous fat emulsion therapy on glyphosate-surfactant-induced cardiovascular collapse. Am J Emerg Med 2012;30:2097.e1–2.
73. Yurtlu BS, Hanci V, Gür A, et al. Intravenous lipid infusion restores consciousness associated with olanzapine overdose. Anesth Analg 2012;114:914–5.
74. Arora NP, Berk WA, Aaron CK, et al. Usefulness of intravenous lipid emulsion for cardiac toxicity from cocaine overdose. Am J Cardiol 2013;111:445–7.
75. Arslan ED, Demir A, Yilmaz F, et al. Treatment of quetiapine overdose with intravenous lipid emulsion. Keio J Med 2013;62:53–7.
76. Bartos M, Knudsen K. Use of intravenous lipid emulsion in the resuscitation of a patient with cardiovascular collapse after a severe overdose of quetiapine. Clin Toxicol (Phila) 2013;51:501–4.
77. Bologa C, Lionte C, Coman A, et al. Lipid emulsion therapy in cardiodepressive syndrome after diltiazem overdose—case report. Am J Emerg Med 2013;31:1154.e3–4.
78. Ellsworth H, Stellpflug SJ, Cole JB, et al. A life-threatening flecainide overdose treated with intravenous fat emulsion. Pacing Clin Electrophysiol 2013;36:e87–9.
79. Gil HW, Park JS, Park SH, et al. Effect of intravenous lipid emulsion in patients with acute glyphosate intoxication. Clin Toxicol (Phila) 2013;51:767–71.
80. Moon HJ, Lee JW. Availability of intravenous lipid emulsion therapy on endosulfan-induced cardiovascular collapse. Am J Emerg Med 2013;31:886.e1–2.
81. Sivalingam SK, Gadiraju VT, Hariharan MV, et al. Flecainide toxicity–treatment with intravenous fat emulsion and extra corporeal life support. Acute Card Care 2013;15:90–2.
82. Abdi A, Rose E, Levine M. Diphenhydramine overdose with intraventricular conduction delay treated with hypertonic sodium bicarbonate and i.v. lipid emulsion. West J Emerg Med 2014;15:855–8.
83. Abdelmalek D, Schwarz ES, Sampson C, et al. Life-threatening diphenhydramine toxicity presenting with seizures and a wide complex tachycardia improved with intravenous fat emulsion. Am J Ther 2014;21:542–4.
84. Agarwala R, Ahmed SZ, Wiegand TJ. Prolonged use of intravenous lipid emulsion in a severe tricyclic antidepressant overdose. J Med Toxicol 2014;10:210–4.
85. Doepker B, Healy W, Cortez E, et al. High-dose insulin and intravenous lipid emulsion therapy for cardiogenic shock induced by intentional calcium-channel blocker and Beta-blocker overdose: a case series. J Emerg Med 2014;46:486–90.
86. Eren Cevik S, Tasyurek T, Guneysel O. Intralipid emulsion treatment as an antidote in lipophilic drug intoxications. Am J Emerg Med 2014;32:1103–8.
87. Sebe A, Dişel NR, Açıkalın Akpınar A, et al. Role of intravenous lipid emulsions in the management of calcium channel blocker and β-blocker overdose: 3 years experience of a university hospital. Postgrad Med 2015;127:119–24.
88. Calenda E, Dinescu SA. Failure of lipid emulsion to reverse neurotoxicity after an ultrasound-guided axillary block with ropivacaine and mepivacaine. J Anesth 2009;23:472–3.
89. Watt P, Malik D, Dyson L. Gift of the glob—is it foolproof? Anaesthesia 2009;64:1031–3.
90. West P, McKeown NJ, Hendrickson RG. Iatrogenic lipid emulsion overdose in a case of amlodipine poisoning. Clin Toxicol (Phila) 2010;48:293–6.
91. Kiberd MB, Minor SF. Lipid therapy for the treatment of a refractory amitriptyline overdose. CJEM 2012;14:193–7.
92. Kundu R, Almasri H, Moza A, et al. Intravenous lipid emulsion in wide complex arrhythmia with alternating bundle branch block pattern from cocaine overdose. Kardiol Pol 2013;71:1073–5.
93. Bazerbachi F, Rank K, Chan A. Intravenous lipid rescue and ropivacaine systemic toxicity. J Anesth 2014;28:139.
94. Downes MA, Calver LA, Isbister GK. Intralipid therapy does not improve level of consciousness in overdoses with sedating drugs: a case series. Emerg Med Australas 2014;26:286–90.
95. Rodríguez B, Wilhelm A, Kokko KE. Lipid emulsion use precluding renal replacement therapy. J Emerg Med 2014;47:635–7.
96. Fettiplace MR, Akpa BS, Rubinstein I, et al. Confusion about infusion: rational volume limits for intravenous lipid emulsion during treatment of oral overdoses. Ann Emerg Med 2015;66:185–8.
97. American College of Medical Toxicology. ACMT position statement: interim guidance for the use of lipid resuscitation therapy. J Med Toxicol 2011;7:81–2.
98. Harrop-Griffiths W, Cave G, Harvey M, et al. AAGBI safety guideline: management of severe local anaesthetic toxicity. London: Association of Anaesthetists of Great Britain and Ireland; 2010.