Intralipid Treatment of Bupivacaine Toxicity

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Background
Cardiac toxicity associated with overdose of intravascular injection of local anesthetic is characterized by hypoten.
atrioventricular conduction delay, idioventricular rhythms, and eventual cardiovascular collapse. Although all loc.
potentially shorten the myocardial refractory period, bupivacaine avidly blocks the cardiac sodium channels, ther.
most likely to precipitate malignant arrhythmias. Even levobupivacaine and ropivacaine (single-enantiomer deriv.
developed to ameliorate cardiovascular side effects, still harbor the potential to disrupt cardiac function.

Data suggest up to 20 out of 10,000 peripheral nerve blocks and 4 per 10,000 epidural blocks result in systemic toxicity. As current practice often favors the addition of regional anesthesia and major plexus blocks to suppleme.
for general anesthesia, all anesthesia professionals must be familiar with signs of local anesthetic cardiotoxicity—
treatment options.

Lipid to the Rescue?
While pretreatment with a lipid infusion in rats was found to increase the dose of i.v. bupivacaine required to indu.
sequent studies examined resuscitation in dogs with lipid emulsion after an intravenous dose of bupivacaine.
found substantially improved hemodynamics and myocardial metabolism. Thus, by 2006, many touted “lipid res.
anesthetic cardiotoxicity and suggested that anesthesiologists routinely stock lipid emulsions wherever regional ar.
practiced. Some challenged these conclusions on grounds that severe systemic toxicity from local anesthetics occ.
greater frequency than is published in medical literature, and that the most appropriate way to limit the hazards of.
anesthetics is to prevent complications with proper injection techniques and careful dosing.

Case Reports Document Lipid Rescue
One case report describes a 58-year-old man who, 30 seconds after an interscalene injection, developed a tonic-cl.
and cardiac arrest. Prolonged ACLS failed to restore a perfusing rhythm, so 100 mL of 20% Intralipid was rapidl.
maintaining cardiac compressions and preparing for cardiopulmonary bypass. Remarkably, the first defibrillation.
administration restored a sinus rhythm, and cardiovascular performance now responded to inotropes and vasopres.
0.5 mL/kg/min was infused for 2 hours, during which time the patient regained full consciousness and recovered.
neurological sequelae. While this case suggests lipids might be routinely stocked in areas in which peripheral ne.
performed, the high-dose safety profile of Intralipid is unknown, and other questions also remain:

1. What is the mechanism of action of lipid rescue?
2. Is the beneficial effect of Intralipid promoted or hindered by concurrent drug therapy administered via ACLS

Currently, 12 published cases support lipid rescue in the setting of local anesthetic cardiotoxicity, where early ad.
 Intralipid is emphasized. Fortunately, it appears that the beneficial effect of Intralipid administration also include.
anesthetics other than bupivacaine.

Proposed Mechanisms
The mechanism by which lipids reverse local anesthetic cardiotoxicity may be increasing clearance from cardiac nonspecific, observed extraction of local anesthetics from aqueous plasma or cardiac tissues is termed a “lipid sink.” Proposed mechanism is that lipids counteract local anesthetic inhibition of myocardial fatty acid oxidation, thereby energy production and reversing cardiac depression.

**Caution is Still Prudent**

The ultimate role of lipid rescue is still debated as some suggest that successful resuscitation could be due to spurious clearance of the instigating local anesthetic within 20 minutes of routine ACLS. Others caution that prevention is appropriate—and the concept of a “remedy” could make some practitioners less careful. Moreover, while lipid is the driving force behind successful cardiac resuscitation, the risk to the brain from prolonged circulatory collapse thus we emphasize that primary therapy remains adherence to proven guidelines—cardiac and SpO2 monitoring, availability and dosing of all local anesthetics, immediate means to support ventilation, proper cardiac compressions CPR, and application of proven advanced life support techniques. Only then should lipid rescue be considered in therapeutic algorithm.

**What Should Clinicians Conclude?**

Assertion of a unique role for Intralipid with new ACLS protocol guidelines must be tempered by awareness that appropriate dose of Intralipid for resuscitation remains unknown and that excess lipid may interfere with lipophilic drugs. Current doses vary widely, and pediatric dosing recommendations are even more elusive. Nonetheless, in a completed in 2006, respondents from 90 academic anesthesiology departments revealed that 26% would consider a rescue in the setting of local anesthetic toxicity—and that the more major nerve blocks performed at an institution likely they were to use lipid rescue. Thirty-nine percent of institutions stored Intralipid in the OR pharmacy, 35% hospital pharmacy, 22% in the “code box,” and 4% in a drug-dispensing device in the OR. More than half of the respondents specified that the drug was accessible in less than 10 minutes. The Association of Anaesthetists of Great Britain a recently provided members with protocols to treat local anesthetic cardiotoxicity that include an infusion of lipid in an editorial published in *Anesthesia & Analgesia*, Brull explains, “based on the available data, it would seem reasonable to have a [lipid] rescue kit available in any setting in which regional anesthesia is practiced—and, in fact, in any location anesthetics are administered by any professional, by any route, and in almost any dose.” Moreover, it will be critical for further investigation of lipid rescue.

Thus, anesthesia professionals should consider this alternative when a patient shows signs and symptoms of local toxicity with, or even before, failing CPR. A useful website, www.lipidrescue.org, is dedicated to the discussion of lipid emulsion reversal of local anesthetic systemic toxicity. Here, the latest data and case reports are synthesized and caution that human prospective studies have not yet been reported, so a registry of local anesthetic-associated arrests is being planned. Indeed, acknowledging the limited understanding of lipid therapy, many questions remain:

- Should the lipid dose be titrated, by patient weight, local anesthetic dose, or the symptoms/signs/severity of toxicology?
- What is the best rate and total dose of the infusion that follows bolus dosing? Is there a safe upper limit of lipid infusion?
- How long should the patient receive the lipid infusion?
- What is the risk of reoccurrence of toxicity once the lipid infusion is stopped?
- Should lipid emulsion be used for patients exhibiting signs of CNS toxicity, or should intralipid only be used to treat cardiac toxicity?
• What are the possible complications or adverse effects of lipid infusion?
• Should lipid be used alone or in combination with epinephrine, and other components of standard resuscitation?
• What is better, 20% or 30% lipid? What formulation is best?
• Intralipid has been used predominantly so far, but is there a better choice?
• Do the other available lipid emulsions work as well?

With all the limitations noted above, one plausible dosing application to consider after “all standard resuscitation to re-establish sufficient circulatory stability” would be as follows:

**20% Intralipid:**

1. Administer 1.5 mL/kg as an initial bolus; the bolus can be repeated 1-2 times for persistent asystole.
2. Start an infusion at 0.25 mL/kg/min for 30-60 minutes; increase infusion rate up to 0.50 mL/kg/min for refractory hypotension.1,10

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References


