Local anesthetic toxicity remains a clinical concern when performing regional anesthesia. Because signs and symptoms of toxicity may not appear for 20 to 30 minutes after administration of local anesthetic, vigilance is crucial. When signs and symptoms of local anesthetic toxicity appear, traditional standards mandate resuscitative measures, including maintenance of oxygenation, elimination of seizures, and treatment of cardiac arrhythmias. However, intravenous administration of lipid emulsions may offer a viable adjunctive treatment of local anesthetic toxicity. The number of case reports demonstrating successful use of lipid emulsions is growing. Continued research remains pivotal to improve understanding of the theory of lipid emulsion pharmacology and application to clinical practice.

**Keywords:** Lipids, local anesthetic overdose, local anesthetic toxicity.

Over the past 12 years, animal research and human case reports offer growing evidence supporting the use of lipid emulsions for patients experiencing local anesthetic toxicity. Lipid research originating with the work of Weinberg and colleagues determined that local anesthetic-induced cardiotoxicity was treated effectively with 10%, 20%, and 30% lipid emulsions. Animal studies using rats and dogs determined that pretreatment or resuscitation with lipid emulsions for bupivacaine overdose offered successful recovery. Specifically, the dog studies demonstrated a return of normal sinus rhythm and baseline blood pressures using lipid emulsions after bupivacaine-induced asystole. Because of the inability to perform human experimental studies, the evidence for the use of lipid emulsions is in case reports. Beneficial effects of the use of lipid emulsions for the treatment of local anesthetic toxicity are documented in case reports beginning in 2006.

In 2006, the first published case report detailed the successful resuscitation of local anesthetic toxicity using intravenous (IV) lipids. After administration of bupivacaine and mepivacaine for an interscalene block, a 58-year-old man showed signs and symptoms consistent with local anesthetic toxicity. Efforts to resuscitate the patient using cardiopulmonary resuscitation failed while preparation began for cardiopulmonary bypass. A 20% lipid emulsion bolus and infusion were begun approximately 30 minutes after the onset of cardiopulmonary resuscitation. The patient was successfully resuscitated. Similarly, an 84-year-old woman was successfully resuscitated with lipid emulsions after administration of an axillary block using ropivacaine. Lipids were begun approximately 10 minutes after initiation of cardiopulmonary resuscitation.

In contrast to the previous case reports, a 91-year-old man admitted for olecranon bursitis surgery received an infraclavicular brachial plexus block using 30 mL of mepivacaine and supplemented with 1% prilocaine using an axillary approach. Because the patient complained of dizziness, nausea, and agitation, he received oxygen and dolastrone (12.5 mg IV). A lipid emulsion bolus of 1 mL/kg was given and repeated after 3 minutes, followed by a continuous infusion. Although ventricular ectopy was apparent, the patient stabilized and regained consciousness within 5 minutes after initiation of lipid emulsion therapy.

Ludot and colleagues recently reported the successful resuscitation of a pediatric patient from local anesthetic toxicity. Approximately 15 minutes after administration of 1% lidocaine with epinephrine and 0.75% ropivacaine for a lumbar plexus block, a wide complex ventricular tachycardia developed in 13-year-old anesthetized girl. A bolus of 20% lipid emulsion was administered as the sole treatment, with successful results.

The case reports demonstrate differences in the timing and amount of lipid emulsions used, types of local anesthetic used, and peripheral nerve block approaches used. Advanced cardiac life support (ACLS) remains the standard protocol for resuscitation of patients after local anesthetic toxicity. The use of lipid emulsions should be considered in the face of local anesthetic toxicity after institution of ACLS. Although differences exist among the existing case reports, adding lipid emulsions to the ACLS protocol resulted in successful outcomes. Similar to the published case reports, the case report that follows describes the successful use of lipid emulsions for an 83-year-old woman who experienced cardiovascular collapse after a femoral sciatic nerve block with bupivacaine and ropivacaine.

**Case Summary**

An 83-year-old, 70-kg woman, ASA physical status II,
was admitted for a total knee arthroplasty. The proposed anesthetic plan consisted of the preoperative administration of both a femoral and sciatic nerve block for postoperative pain management and the use of a subarachnoid block for operative anesthesia. The patient’s medical history included severe osteoarthritis. The patient was otherwise healthy and lived independently. She took daily vitamins and nonsteroidal anti-inflammatory medications. Preoperative laboratory tests and chest radiographs were within normal limits. Preoperative vital signs included a blood pressure of 118/58 mm Hg, heart rate of 69/min, oxygen saturation of 100%, and an electrocardiogram (ECG) demonstrating a normal sinus rhythm. Because of the patient’s advanced age, the orthopedic surgeon ordered a stress test, which demonstrated a consistent normal sinus rhythm without ectopy and no evidence of myocardial ischemia.

The patient was admitted the day of surgery and consented to the femoral sciatic nerve block with sedation. After placement of standard monitors, including ECG, blood pressure, and pulse oximeter, and placement of an IV access, the nerve blocks were performed. The patient was sedated with midazolam (Versed), 3 mg, and fentanyl, 100 µg IV. In the preoperative holding area, a femoral nerve block was performed uneventfully using a 10-cm, 18-gauge, Tuohy insulated stimulating needle. Careful placement included aspiration to avoid intravascular injection. A 20-gauge insulated catheter was threaded for postoperative analgesia. Bupivacaine 0.5% with epinephrine 1:200,000 (15 mL) and 1% ropivacaine (15 mL) were slowly injected. Immediately after the femoral nerve block, the patient was repositioned and a sciatic nerve block was performed using a 90-mm, peripheral nerve block, B-bevel, 20-gauge needle (StimuQuik, Arrow International Inc, Reading, Pennsylvania). Bupivacaine 0.5% with epinephrine 1:200,000 (15 mL) and 1% ropivacaine (15 mL) were again slowly injected after careful aspiration. Vital signs remained stable throughout the peripheral nerve block placement, and the patient showed no signs of distress.

Approximately 5 to 10 minutes after the sciatic nerve block, the patient’s vital signs deteriorated, which included a profound bradycardia (30 to 40/min) and a declining blood pressure (60 to 70 mm Hg systolic with palpable femoral pulses). The ECG changes progressed from a first degree heart block to complete heart block with multifocal ventricular beats (Figure 1). Wide complex ventricular tachycardia appeared after administration of atropine, 1 mg IV. Because the patient was sedated, no central nervous system changes were noted by the Certified Registered Nurse Anesthetist (CRNA) who remained in the preoperative area after the block. The patient was unresponsive to verbal commands and began to have seizures. Intravenous midazolam, 4 mg, was given immediately. With the help of a second CRNA, the patient was ventilated by mask with 100% oxygen and was intubated, and ACLS protocol was followed for resuscitation. Pacemaker pads were placed. Approximately 5 minutes after initiation of the ACLS protocol, a 20% IV lipid emulsion (Liposyn) at a 250-mL dose was

Figure 1. Clinical Deterioration 5 to 10 Minutes After Administration of Local Anesthetic
infused rapidly over 30 minutes, followed immediately by a second 250-mL infusion. Although case reports demonstrate using lipid emulsion bolus dosing, recommended dosing schedules had not been previously examined. This was an initial experience using lipid emulsions to treat local anesthetic toxicity. Approximately 4 to 5 minutes after the lipid emulsion infusion, cardiac electrical activity indicated a wide complex intraventricular tachycardia followed by normal sinus rhythm (Figures 2 and 3). Oxygen saturation remained at 98% to 100% with effective mask ventilation and subsequent intubation. The blood pressure and heart rate returned to the patient’s baseline values. Over the next 4 hours, the patient’s vital signs remained stable while she was mechanically ventilated and sedated in the intensive care unit (ICU). The ECG demonstrated a consistent normal sinus rhythm (Figure 4). The patient was extubated a few hours after admission to the ICU and discharged to home the next morning without further sequelae. Approximately 3 weeks later, the patient returned to the rural community hospital for a total knee arthroplasty using an uneventful spinal anesthetic.

Discussion

Local anesthetic toxicity remains a peril associated with regional anesthesia. The incidence of local anesthetic toxicity ranges from 7.5 to 20 per 10,000 peripheral nerve blocks and about 4 per 10,000 epidural blocks; however, the incidence may be underreported. Treating local anesthetic toxicity includes ensuring oxygenation and treatment of cardiovascular collapse using ACLS protocols. Before the use of lipid emulsions, patients with failed cardiac resuscitation required life support including cardiopulmonary bypass. Although case reports offer substantive evidence supporting the usefulness of lipid emulsions for local anesthetic toxicity, a review of the literature lacked evidence demonstrating failed attempts of resuscitation using this innovative approach.

The case reported herein adds to the existing list of case reports supporting the successful use of lipid emulsions for suspected local anesthetic toxicity. Suspected local anesthetic toxicity for this sedated patient manifested through the unresponsiveness, seizures, and cardiovascular collapse consistent with high local anesthetic peak plasma concentrations possibly due to excessive dose, particularly for this octogenarian. Vigilance and prompt intervention by the CRNAs facilitated timely ACLS protocol and the decision to use lipid emulsions. The presence of the ECG technologist in the preoperative area offered the ability to record serial ECGs providing additional evidence of change in cardiac electrical conductivity after lipid emulsion infusion.

Lipid emulsions are composed of 20% soybean oil, 1.2% egg yolk phospholipids, 2.25% glycerin, and water. Various commercial preparations are available. Although the exact mechanism of action is unknown, several theories exist regarding how lipid emulsions counteract the negative effects of local anesthetic toxicity. The mechanism of a “lipid sink” suggests that a large serum lipid phase extracts local anesthetics from the plasma. Binding the lipid-soluble local anesthetic may reduce the overall plasma local anesthetic concentration. Recent research using bupivacaine, levobupivacaine, and ropivacaine demonstrated binding ability to lipid emulsions, further supporting the lipid sink theory and use in local anesthetic toxicity. In addition, lipids may foster cardiac metabolism by augmenting the fatty acid supply, promoting aerobic metabolism and reducing acidosis.

When used to treat local anesthetic toxicity, side effects of lipid emulsions have not been reported. However, side effects are possible with long-term use of lipid formulations for nutritional purposes. Disorders associated with fat metabolism as well as egg allergies remain contraindications for use of lipid emulsions. In addition to risk of infection, allergic reactions, fat emboli, altered mental status, and increased intracranial pressure may result with long-term use of lipid emulsions. However, because of the short-term use of lipid emulsions in treating local anesthetic toxicity, allergic reaction remains the primary potential side effect.

Because case reports support the use of lipid emulsions in cases in which local anesthetic toxicity is suspected, some authors have recommended having lipid emulsions available. Procurement of lipid emulsions in areas where regional anesthesia is frequently performed remains essential for prompt intervention. Early recommendations suggested that cardiopulmonary resuscitation commence, followed by administration of lipid emulsions. The cases reported in the literature reflect a shortened interval from the onset of the signs and symptoms of local anesthetic toxicity to initiation of lipid therapy. In cases of local anesthetic toxicity, prompt administration necessitates the availability of lipid emulsions, particularly in the operating room, labor and delivery, and areas where regional blocks are placed. For the case reported here, the small community hospital maintains a supply of 20% Liposyn. However, previous to this case, the CRNAs caring for the patient had no personal experience using lipid emulsions for treatment of local anesthetic toxicity.

Research regarding dosing continues to evolve. The suggested dosing regimen for lipid emulsions based on case reports of local anesthetic toxicity is a 1.5-mL/kg bolus of 20% lipid emulsion solution, followed by a 0.25-mL/kg per minute infusion for 30 to 60 minutes. The bolus may be repeated 1 or 2 times for continued asystole. If the blood pressure continues to decline, increasing the infusion rate is suggested. Although a bolus dose was not used for the patient in this case report, the lower-than-recommended dose facilitated
promising ECG changes. However, for future use, a bolus dose followed with the infusion would be used because considerable case report information and dosage guidelines remain readily available. Like dosing information required for the use of dantrolene for malignant hyperthermia, dosing information for lipid emulsions should be available in areas where local anesthetics are used.
Conclusion
For the patient in this case report, CRNA vigilance allowed prompt intervention aimed at ameliorating the signs and symptoms of suspected local anesthetic toxicity with return to normal cardiovascular function. Although ACLS protocols were instituted, cardiovascular decline ensued. Readily available lipid emulsions offered a viable adjunct in the treatment of suspected local anesthetic toxicity for the patient. Lipid emulsions should be considered as an adjunct to resuscitative efforts when local anesthetic toxicity is suspected. The suggested dosing regimen for lipid emulsions based on local anesthetic toxicity case report evidence includes a 1.5-mL/kg bolus of 20% lipid emulsion solution, followed by a 0.25-mL/kg per minute infusion for 30 to 60 minutes. The bolus may be repeated 1 or 2 times for continued asystole.

The list of case reports demonstrating successful resuscitation for patients with local anesthetic toxicity continues to grow, offering further support for the use of lipid emulsions. Additionally, evidence from case reports suggests the usefulness of lipid emulsions to counteract the effects of other lipid-soluble substances, including overdose from psychotropic medications. Because of the growing evidence supporting the use of lipid emulsions, continued research regarding their use and efficacy is warranted. Additionally, the optimal dosing regimens and when to start lipid emulsion therapy merit further study.

REFERENCES

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