

## Lipid Emulsion in the Successful Resuscitation of Local Anesthetic Toxicity after Ankle Block

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Unexpected occurrence of local anesthetic toxicity is not rare and can cause fatal complications that do not respond to any known drug of intervention. Recently, the successful use of lipid emulsion for local anesthetic toxicity has been reported and recommended as a rescue method for cardiac or neurologic complications. We report a case of seizure attack and respiratory arrest successfully recovered with the use of intravenous lipid emulsion. Clinicians must be aware of the beneficial role of lipid emulsion in cases of local anesthetic toxicity.

**Key Words:** anesthetics, local; antidotes; intravenous lipid emulsions; neurotoxicity syndromes.

Local anesthetics overdose can lead to threatening situations for its neural and cardiotoxicity which is refractory to conventional resuscitation. Recently, many cases about reversal of local anesthetic toxicity caused by lipid emulsion have been reported showing the possibility of a new protocol.[1] We experienced a case of recurrent convulsion and respiratory arrest after ankle block using lidocaine and bupivacaine, and lipid emulsion administration could cease the neurotoxicity syndrome.

### Case Report

A 59-year-old woman (height 159 cm, weight 56 kg) was scheduled for secondary left distal metatarsal chevron osteotomy

due to right hallux valgus. She had undergone the same operation under sciatic nerve block using bupivacaine uneventfully. Her medical history included well-controlled hypertension and a cerebral vascular accident without any symptoms for the last 10 years. The brain MRI finding after admission revealed no defective lesion. Routine laboratory data, electrocardiogram, and chest radiograph revealed no serious abnormalities.

Her vital signs on arrival at the operation room were 120/80 mmHg of blood pressure (BP), 86 beats/min of heart rate (HR), 24 breaths/min of respiratory rate, and 99% of oxygen saturation by pulse oxymetry (SpO<sub>2</sub>) on room air. She received 3 L/min of oxygen with nasal cannula. A 20-gauge intravenous catheter was placed in her left forearm and 25 mg pethidine and 2 mg midazolam were administered for an appropriate level of sedation. The left ankle block was performed via a three-point injection including deep peroneal nerve, posterior tibial nerve, and sural nerve. A 10 ml of 2% lidocaine and 10 ml of 0.5% bupivacaine mixture was injected after repeated negative aspiration test. Five minutes later, the sensation in the left great toe remained. Additionally, the same dosage of the mixture was injected into the same points.

Ten minutes later, she became restless, groaned, breathed with difficult and convulsed in a tonic clonic seizure. But her vital

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signs were in normal range and EKG had shown sinus rhythm. She was supported by a facial mask with intermittent positive pressure ventilation delivering 100% oxygen. 200 mg of pentotal sodium was given intravenously to stop seizure activity. The seizure promptly ceased, but apnea immediately followed. However, the airway was not fully secured, and arterial blood gas analysis indicated hypoventilation (pH 7.01, PCO<sub>2</sub> 80 mmHg, PO<sub>2</sub> 77 mmHg, HCO<sub>3</sub> 20.2). As a result, an additional 100 mg of pentotal sodium and 50 mg of succinylcholine were given for endotracheal intubation. The secondary seizure developed and terminated in a minute after injection of 2 mg of lorazepam. The patient was transferred to the intensive care unit.

On arrival at the intensive care unit, the patient was supported by mechanical ventilation. Her vital signs were stable (121/84 mmHg of BP, 60 beats/min of HR, 100% of SpO<sub>2</sub>) but the Glasgow coma scale was 3 without any response for pain stimuli. To prevent the relapse of convulsion and to reverse the local anesthetics toxicity, prolonged respiratory depression and decreased consciousness due to unintended intravascular injection, 20% Intralipid (Baxter Pharmaceuticals, Fresenius Kabi, Uppsala, Sweden) was injected as a bolus (90 ml for one minute, approximately 1.5 ml/kg) followed by a continuous infusion of 15 ml/min (0.25 ml/kg/min) for 30 minutes. After a total infusion of 540 ml of lipid emulsion, she responded to pain sensation. The vital signs and arterial blood gas analysis maintained within normal range with continuous positive airway pressure mode, and she was fully awake and extubation was done 3 hours later. Neurologic sequelae had not been sustained nor complication secondary to intralipid administration. The patient was discharged 3 days later, and no complications were reported.

## Discussion

Local anesthetics are widely used for regional anesthesia because of their simplicity and ability to facilitate fast recovery. However, local anesthetics' complication is not rare. In particular, peripheral nerve block is associated with the highest incidence of systemic toxicity (7.5/10,000 persons),[2] and it can cause serious side effects such as disorientation, generalized convulsion, cardiovascular collapse and difficult resuscitation. Furthermore, bupivacaine is more likely than other local anesthetics to be responsible for serious central nervous system toxicity for its lipophilicity and prolonged acting-time.[3] In this case, total anesthetics dosage was lower than the clinical maximal dosage for nerve block, 500 mg of lidocaine and 225 mg of bupivacaine,[4]

but seizure and respiratory depression were followed by additional injection of local anesthetics. Toxicity of local anesthetics followed by incidental intravenous injection was suspected. Even though the first seizure was ceased by benzodiazepine, the secondary seizure re-occurred and self respiration disappeared. Finally, we decided to administer lipid emulsion.

The successful lipid emulsion usage for refractory cardiac arrest after brachial plexus block with bupivacaine was reported for the first time by Rosenblatt et al.[5] Also, several cases about reversal of cardiac and neurologic toxicity by local anesthetics using lipid emulsion were reported.[6-8] Oda and Ikeda[9] found that higher doses and concentrations of lipid binding bupivacaine were required to induce convulsion and cardiac arrest than those of free bupivacaine in rats. But it is not clear how lipid emulsion reverses the toxicity of local anesthetics. Recently, the "lipid sink" mechanism has explained that lipid globules surrounding bupivacaine creates decreased bupivacaine concentration.[10] Kuo and Akpa[11] had described the reduction of the tissue bupivacaine concentration by lipid binding through physiologically based pharmacokinetic (PBPK) model, and as the result the concentration of brain tissue could be reduced by 18% within the first 15 minutes. Another alternative theory is suggested about direct inotropic effect of lipid infusion. Stehr et al.[12] reported the significant positive inotropic effects after lipid application in the case of cardiac depression by bupivacaine. Guidelines for the use of lipid emulsion in resuscitation of local anesthetic toxicity have been introduced through the American Society of Regional Anesthesia (ASRA) and the American Heart Association.[13] The recommended direction is initial intravenous bolus of 20% lipid emulsion (approximately 1.5 ml/kg of lean body mass) immediately followed by continuous infusion (approximately 0.25-0.5 ml/kg/min) for roughly 10 minutes until recovery of vital signs appears.[14]

In this case, a larger dosage of infused lipid emulsion due to longer duration (30 minutes) than recommended by ARSA caused concern about the complications of lipid emulsion overdose. Some adverse effects of lipid emulsion have been reported including thrombophlebitis, seizure, immune dysfunction and lipid emboli to the splenic, cerebral, pulmonary circulation.[15-17] Although its effects are transient, the incidence of lipid emboli may be related to the volume and rate of infusion, moreover it is associated with a rate exceeding 0.5 ml/kg/h of 20% intravenous lipid emulsion, which is less than the therapeutic dose of lipid emulsion.[18] However, Ozcan and Weinberg[19] reported that the lipid emulsion usage protocol of 1.5 ml/kg bolus plus 0.2-0.5 ml/kg/min for 10-30 minutes had not evoked any complications. And West et

al.[20] reported that any complication of lipid emulsion was not detected in the case of overdose, which uses 2,000 ml of 20% intravenous fat emulsion over 4.5 hours (8.9 ml/kg/h).

In conclusion, clinicians should understand and cope with the local anesthetic toxicity after peripheral nerve block. Also, the protocol about usage of lipid emulsion should be known well. For its moral problem, local anesthetic toxicity and lipid emulsion efficacy can never be subjected to controlled trials, so it is important that many cases are reported and shared to reveal the efficacy and risk of the intervention that can become a part of accepted practice. Some experiences are posted at <http://www.lipidrescue.org/> by ASRA recommendation, and many case reports and laboratory data have been published supporting this intervention, which needs more exact back-up data and supplementation.

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