CASE REPORT

The Successful Use of Intralipid for Treatment of Local Anesthetic-induced Central Nervous System Toxicity

Some Considerations for Administration of Intralipid in an Emergency

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Abstract: Intralipid has been proposed as a treatment option for local anesthetic (LA) toxicity, which does not respond to traditional resuscitation methods. This paper presents a case report of a patient who developed signs of local anesthetic toxicity and was subsequently treated with 20% Intralipid with a positive response. Some background and practical applications regarding this treatment are discussed.

Key Words: local anesthetic, toxicity, intravenous Intralipid (Clin J Pain 2009;25:808–809)

BACKGROUND

Guy Weinberg was the first person to study and report the use of lipid emulsion treatment for bupivacaine-induced asystole in rats.1 He later reproduced similar results in studies with dogs.2 On the basis of the results of these studies demonstrating successful resuscitation from bupivacaine toxicity in these animals, it was postulated that Intralipid could be used in humans for resuscitation from local anesthetic toxicity.

A few human case reports now exist demonstrating use of Intralipid 20% where local anesthetic (LA) has caused central nervous system toxicity.3–5 We would like to add a case to the literature regarding the successful use of Intralipid in the treatment of LA-induced central nervous system toxicity.

CASE

A 36-year-old 80 kg man developed signs and symptoms of local anesthetic toxicity after undergoing a lower leg nerve block. The patient had a history of chronic right leg pain as a previously sustained injury from a fall 3 years previously. He was placed in a leg cast but subsequently developed a femoral-popliteal deep vein thrombosis and a lower limb compartment syndrome, requiring fasciotomy and myomectomy of his gastrocnemius. The painful spasms of the leg began approximately 4 months after the injury and operation for compartment syndrome. The muscle spasms were clearly seen to be involving the muscles of the lateral compartment of the leg with the foot and toes becoming everted or inverted depending on the muscle groups involved at the time of the spasm. The patient received full medical assessments by neurologists and orthopedists and had nerve conduction and electromyography studies performed. These showed injury with axonal degeneration of the common peroneal nerve and the sciatic nerve just above the right knee joint, confirming a neuropathic etiology for his pain. A surgical decompression and neurolysis of the popliteal nerve carried out on this admission demonstrated that the nerve was flattened and scarred. As part of the comprehensive assessment of the pain, the patient had a full psychiatric evaluation performed, which revealed anxiety of the patient about the situation, but this was not thought to be a contributor to the etiology of the problem.

On admission, his presentation involved intractable pain and spasm of the right lower leg involving virtually all muscle groups innervated by the common fibular and tibial nerves. These spasms were found to be resistant to lignocaine, benzodiazepine or opioid infusions. Over the next 3 weeks he received regular intramuscular local anesthetic injections, intramuscular Botox injections, several nerve blocks, epidural infusions, selective phenol nerve ablations, and eventually had radiofrequency ablations of the tibial and common fibular nerves. In addition, the patient continued to be managed on long-term cloxane (enoxaparin) deep venous thrombosis prophylaxis and various narcotics along with adjuvants (pregabalin and dantrolene) for pain.

On the occurrence of this incident, the patient was injected with a mixture of 10 mL of 1% lignocaine (with adrenaline 1:200,000) and 20 mL of 0.5% bupivacaine into the soleus and extensor hallucis longus muscles for the purpose of pain and spasm relief. Within 60 seconds of administration, the patient developed symptoms including perioral tingling, headache, dizziness, light headedness, diplopia, and these were quickly followed by an elevated heart rate of 153/min and elevated blood pressure (180/110) and ST segment depression in the anterior and lateral chest leads of the electrocardiography. The rapid onset of neurologic symptoms led us to the conclusion that this might be the result of local anesthetic toxicity.

An immediate resuscitation call was made and 1L of Hartmann’s solution was given through intravenous access and oxygen was delivered through a facemask. Within 5 minutes of the event, 20% Intralipid was injected via 100 mL boluses on 2 occasions, with each bolus lasting between 1 to 3 minutes. Within the first minute of administering the Intralipid, the patient’s symptoms dramatically improved, with the heart rate dropping to 92/min and blood pressure of 158/105. The patient’s headache, diplopia and feelings of faintness also subsided quickly. An additional 100 mL was given as an infusion over 1 hour. The patient was admitted to the intensive care unit for observation for 8 hours and then returned to the ward. A repeat electrocardiography at the time of intensive care unit discharge demonstrated a complete reversal of the ST segment pattern seen on the previous tracing.

The therapeutic model as previously proposed by G. Weinberg for cardiac toxicity is 1 mL/kg of 20% intralipid, given over 1 minute while continuing chest compressions, repeated every
Intralipid 20% at a rate of 0.25mL/kg until hemodynamic point or earlier (with evidence of recovery) to a continuous infusion 3 to 5 minutes to a maximum of 3mL/kg and converting at that method of delivery of Intralipid was through a 100 mL dose within the required time. We found the most effective dose of Intralipid available at any site where local anesthetic is considered in cases of local anesthetic toxicity when resuscitation has been unsuccessful.\(^2\)–\(^5\)\(^,\)\(^7\)

Weinberg has a recommended dosing regimen for the treatment of local anesthetic toxicity. However, we found that there were some practical difficulties to the administration of Intralipid that we encountered and believe that the guidelines should include a discussion on how to administer the agent.

Twenty percent of 1000 mL Intralipid contains purified soybean oil 200 g, purified egg phospholipids 12 g, glycercol anhydrous 22 g, and water for injection. The pH is adjusted with sodium hydroxide to approximately 8. The energy content/L is 8.4 MJ (2000 kcal) and the osmolality (approx.) 350 mosmol/kg water. In our hospital, 20% Intralipid is provided in 500 mL glass bottles and is usually accompanied by a calibrated 100 mL burette for administration. When connecting the burette to intravenous canula, we found that the viscous nature of the drug resulted in too slow a delivery of the agent to obtain the calculated bolus dose within the required time. We found the most effective method of delivery of Intralipid was through a 100 mL syringe, pushed into the vein by hand.

In presenting this case study, we have chosen to discuss some of the practicalities of administration of Intralipid whereas previous articles have focused on postulated mechanisms of Intralipid’s action.

The exact mechanism of how local anaesthetic causes cardiotoxicity is not certain, neither is the mechanism of how Intralipid overcomes such effects. Current knowledge indicates that local anaesthetics inhibit voltage and ligand gated channels in addition to some other proteins. In addition, it is possible that acyl carnitine (the transport molecule responsible for transferring fatty acids into the mitochondria) may also be inhibited by local anaesthetic. Postulated mechanisms for the action of Intralipid in the reversal of the toxicity of local anaesthetic include:

1. Acting as a lipid sink, in which LA is drawn into.

Local anesthetic toxicity although uncommon, usually presents as an emergency requiring immediate treatment. We suggest that in addition to having a ready supply of Intralipid available at any site where local anesthetic is being injected, there should also be some consideration given to a delivery system including a supply of large volume syringes (50 or 100 mL) to ensure that the calculated bolus of the agent is given within the time required to be effective.

Despite the clinical excitement, which surrounds the use of Intralipid for the treatment of LA toxicity, it must be borne in mind that there have been reports of adverse effects with its administration, even after single use. Most commonly, these include vein irritation resulting in thrombophlebitis. Less frequently, immediate reactions have been reported to occur in clinical trials, in an incidence of less than 1%. These include dyspnea, cyanosis, allergic reactions, hyperlpaemia, hypercoagulability, nausea, vomiting, headache, flushing, increase in temperature, sweating, sleepiness, pain in the chest and back, slight pressure over the eyes, and dizziness. Delayed adverse reactions such as hepatomegaly, jaundice because of central lobular cholestasis, splenomegaly, thrombocytopenia, leukenopenia, transient increases in liver function tests and pancreatitis have also been reported but are uncommon.

The use of Intralipid to treat other forms of LA toxicity remains unknown and remains a potential area to explore in future papers. However this would need to be performed with animal models before any application can be extrapolated to the human situation.

A review of the literature does not offer effective options, to treat patients with local anesthetic toxicity, who do not respond to traditional resuscitation methods. Intralipid seems to be the best choice currently available to deal with this difficult circumstance. Further case reports could support the use of Intralipid in scenarios where LA toxicity develops.

**REFERENCES**


