

## Lipid Emulsion as First Line Treatment in Ropivacain Induced Neurologic Toxicity

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### Abstract

A 67 year old female patient presented with new neurological deficits (clonic movements, progressive confusion, dysarthria) and hemodynamic instability (hypotension, sinus tachycardia) immediately after uneventful performance of a sciatic block. Prompt infusion of a 100 ml intralipid emulsion in addition to a single bolus of 100 mcg phenylephrine reversed these signs within less than five minutes. Subsequently she remained hemodynamically stable and her neurological status returned to baseline. In absence of further signs of toxicity, the continuous intralipid infusion was interrupted.

### Introduction

Informed consent was obtained from the patient for publication of this case report.

The use of intravenous lipid emulsions in the setting of local anesthetic intoxication has now gained a wide acceptance amongst anesthetists. Although many case reports confirm lipid emulsions are safe to use, most authors recommend administration in presence of cardiac arrest or severe hemodynamic compromise. Current British guidelines recommend the use of lipid emulsions in such instances [1]. Cardiovascular instability due to local anesthetic intoxication is notoriously difficult to reverse. We believe that lipid emulsions should also be administered promptly in presence of milder signs of local anesthetic intoxication. One should not wait for cardiac arrest or severe hemodynamic instability to occur before considering administration of a lipid emulsion. We see no benefit in postponing initiation of a treatment that can potentially prevent severe and refractory cardiac complications if known to be safe.

### Case Description

This is a 67 year old woman, 160 cm tall and weighing 52 kg, who was scheduled for left foot arthrodesis. Anesthetic risk was graded American Society of Anesthesiologists (ASA) 2 due to a personal history of left breast cancer surgically removed by tumorectomy, and a regressive cerebral vascular accident for which she was prescribed aspirin.

7.5 mg oral midazolam was administered before the procedure. Shortly after arrival in the anesthetic area, standard monitoring with a 3-lead continuous ECG, blood pressure cuff on right arm, and pulsed oxymetry was installed in addition to placement of a 20G intravenous catheter on the left forearm. A 1000 ml Lactated Ringer infusion was started. Baseline blood pressure was 120/60 mmHg, pulse 70 bpm, pulsed oxymetry 96% at ambient air. Before the patient was positioned on the right side, 50mcg fentanyl was administered intravenously to maximize the patient's comfort during performance of regional anesthesia. Labat's approach was used for sciatic blockade. A 100 mm insulated needle (Top Neuropole needle-ST, 100 mm 23G, Top corporation, Tokyo, Japan) was connected to a nerve stimulator (Stimuplex HNS 12, B. Braun Melsungen AG, Melsungen, Germany) with a starting output of 1 mA, 1 ms and 2 Hz. Appropriate foot flexion was elicited within one minute and current intensity was reduced until disappearance of motor response at 0.3 mA. After absence of blood on inspiration was confirmed, 20 ml of 0.5% ropivacain were

injected over 2 minutes with repeated aspiration tests at 5 ml intervals. Within seconds after injection of the local anesthetic solution (while the patient was being repositioned supine for femoral nerve blockade), we observed sudden clonic movements of the limb, followed by profound confusion and visual hallucinations. The patient never lost consciousness; she remained aware of her surroundings at all times and could describe her visions of climbing a very steep mountain with great precision. Blood pressure concomitantly dropped to 70/40 mmHg while heart rate accelerated to 96 bpm.

We immediately administered pure oxygen by facemask, injected 100 mcg phenylephrine intravenously, and started a 100 ml single bolus of 20% lipid emulsion over approximately 1 minute. Confusion regressed quickly; within 5 minutes her neurologic and mental status returned to baseline. After initial management, hemodynamics and cardiac electrical activity remained stable without need for further support. The patient remained monitored for about 30 minutes in the anesthetic area; we observed no recurring signs of local anesthetic intoxication and therefore decided to forfeit the recommended lipid infusion maintenance dose. Instead, a second lipid emulsion was kept ready for infusion in case of recurring symptoms of local anesthetic toxicity. We monitored ropivacain blood levels with samples drawn 20 and 50 minutes after local anesthetic injection. Measured levels were 1.9 mg/l (6.94  $\mu$ mol/l) and 1.4 mg/l (5.02  $\mu$ mol/l) respectively. Testing for superficial sensation to cold using a cold pack confirmed presence of an efficient sciatic block despite normalization of both neurologic and cardiac functions. We decided not to perform any femoral block as previously planned to improve comfort during tourniquet inflation. After discussion with the surgeon in charge, we decided to proceed with the scheduled operation. Sciatic blockade proved insufficient; we had to induce general anesthesia with 300 mg pentothal, 75 mg succinylcholine, 150 mg fentanyl. An orotracheal tube was inserted. The rest of the procedure was unremarkable.

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## Discussion

In this case, local anesthetic intoxication happened despite multiple negative aspiration tests. The underlying mechanism may involve a rapid systemic absorption of a large amount of ropivacain (very uncommon during sciatic blockade) or, more likely, an undetected intravascular injection. The subsequent insufficient anesthesia provided by the sciatic block and the high measured concentrations of ropivacain (1.9 mg/l) tend to support the latter hypothesis. Such concentrations have been shown to be associated with appearance of neurological signs in healthy volunteers [2]. Concomitant hypotension and tachycardia are known early signs of cardiac toxicity [3]. Since lipid emulsion infusion had already been started at time of sampling, we cannot report peak plasmatic concentration of ropivacain before beginning of therapy.

Given the course of events, it seemed reasonable to immediately suspect local anesthetic intoxication as being causative of the clinical picture. Although neurologic signs were moderate and cardiac impairment easily treatable, it was clear we were in the presence of a potentially dangerous intoxication. We therefore decided to administer 100 ml of a 20% lipid emulsion in anticipation of further compromise.

Lipid rescue has achieved a large acceptance in the setting of local anesthetic intoxication. Since Weinberg first demonstrated beneficial effects of lipid infusions in rats [4], several reports have confirmed their usefulness and safety in presence of life threatening cardiac dysfunction such as ventricular fibrillation with cardiac arrest [5,6], or other severe acute arrhythmias [7]. Current guidelines recommend the use of lipid emulsions during resuscitation only [1].

Recent concerns about a potential risk of acute pancreatitis induced by the sudden high load of intravenous lipids [8] must be acknowledged. Some authors suggest practitioners should weigh out the risk of inducing a potentially lethal iatrogenic complication as long as expected benefits of lipid infusions are not firmly established [9]. Additionally, Harvey et al. [10] demonstrated impaired recovery of spontaneous circulation with lipid infusion following severe myocardial ischemia using an animal model that was later supported by similar results [11]. Of note, the cardiotoxic effects of local anesthetics may outlast the protection offered by the initial lipid bolus [8]. Guidelines recommending the administration of a continuous infusion of lipids following the initial bolus stem from this observation. Total infusion volume may reach up to 500 ml. The precise clinical implications of such high volumes of lipids are not established yet.

We believe an intravenous lipid emulsion should be promptly started as soon as local anesthetic intoxication is suspected. Charbonneau et al. were confronted to a similar case of neurological dysfunction after brachial plexus blockade. Immediate administration of a lipid emulsion was followed by complete resolution of neurological signs [12]. We see little to no gain in waiting for more serious signs to occur before starting therapy. In our opinion, the ability of lipid emulsions to prevent severe cardiac complications outweighs the potential risk of hyperlipidemia. In any case, lipid emulsions should clearly be administered without delay in cases of cardiac arrest following regional nerve blockade using local anesthetics.

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## Implications Statement

We suggest that, in the setting of local anesthetic intoxication, infusion of a

lipid emulsion should be administered as early as possible. Whenever possible, it should be started before evidence of cardiovascular instability.

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