Recurrence of Cardiotoxicity After Lipid Rescue from Bupivacaine-Induced Cardiac Arrest

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Accidental intravascular administration of bupivacaine during performance of a brachial block precipitated convulsions followed by asystole. The patient was rapidly resuscitated using cardiopulmonary resuscitation, supplemented by 150 mL of 20% lipid emulsion. Nonetheless, cardiac toxicity reappeared 40 min after completion of the lipid emulsion. In the absence of further lipid emulsion, amiodarone and inotropic support were used to treat cardiotoxicity. This case suggests that local anesthetic systemic toxicity may recur after initial lipid rescue. Since recurrence of toxicity may necessitate administration of additional doses of lipid emulsion, a sufficient quantity of lipid emulsion should be available when regional anesthesia is performed.

(Anesth Analg 2009;108:1344–6)

The use of lipid emulsions to treat systemic local anesthetic toxicity has recently been highlighted in case reports[1–9] and editorials.[10–16] We present a case of lipid rescue in which systemic toxicity recurred 40 min after successful treatment with lipid emulsion.

CASE REPORT

A 33-yr-old man (72 kg, 168 cm) presented for debridement of a compound fracture of his right humerus. The patient's vital signs, clinical examination, preoperative hemoglobin concentration and urine analysis were unremarkable.

A single injection infraclavicular paracoracoid block was performed after placement of an 18-gauge ported IV cannula. No sedation was administered. The brachial plexus was located using a 50 mm insulated needle (Stimuplex®, B Braun, Melsungen, Germany) attached to a nerve stimulator (Neuro-Trace III®, HDC® Corporation, Milpitas, CA). Evoked responses of finger and wrist flexion were first elicited at 2 mA and disappeared at 0.4 mA. After injection of 30 mL of 0.375% bupivacaine hydrochloride without epinephrine (Micro Healthcare, Bethlehem, South Africa) over 3 min, with aspiration at 5 mL intervals, the patient abruptly reported the new onset of a dry sensation in his throat and eyes. These symptoms prompted immediate cessation of local anesthetic injection and removal of the insulated needle. This was immediately followed by generalized convulsions and apnea. Facemask intermittent positive pressure ventilation delivering 100% oxygen was initiated. Intralipid® (Fresenius Kabi®, South Africa) that was held in the postanesthesia care unit was available within 30 s of the onset of convulsions. Convulsions were terminated within 60 s by the administration of IV thiopental, 100 mg succeeded by a further 150 mg.

After termination of convulsions, the electrocardiogram trace became visible and revealed a narrow complex tachycardia, which accelerated to a peak rate of 160 bpm. Over 90 s, the tachycardia was succeeded by broadening of the QRS complexes, slowing of the heart rate and asystole.

Intralipid 150 mL was administered over approximately 90 s, the infusion commencing just prior to asystole. External cardiac compressions were begun, tracheal intubation was performed and epinephrine 1 mg was administered IV. During cardiopulmonary resuscitation, capnography (Dräger®, Lübeck, Germany) recorded an end-tidal carbon dioxide partial pressure (P_{ETCO_2}) of 19 mm Hg.

Within 3 min of completing the first 150 mL of lipid emulsion, the patient converted from asystole to a narrow complex rhythm at 130 bpm. This rhythm was associated with an arterial blood pressure of 160/120 mm Hg, P_{ETCO_2} of 61 mm Hg and an oxygen saturation (as measured by pulse oximetry) of 100%. Analysis of arterial blood samples obtained from a radial arterial catheter 5 min after return of spontaneous circulation revealed a pH <6.8, $Paco_2$ 113.3 mm Hg, Pao_2 180 mm Hg, lactate more than 15 mmol/L, potassium 3.2 mmol/L and glucose 10.9 mmol/L. Repeat analysis 11 min after return of spontaneous circulation revealed similar values, albeit $Paco_2$ had decreased to 55 mm Hg. The blood gas analyzer could not estimate bicarbonate levels nor base deficit. These measurements prompted an increase in minute ventilation and IV administration of sodium bicarbonate, insulin, and potassium. A further blood gas analysis 110 min after return of spontaneous circulation revealed pH 7.30, $Paco_2$ 53 mm Hg, Pao_2 257 mm Hg, bicarbonate 21.0 mmol/L, base deficit 5.2, lactate 8.5 mmol/L, potassium 2.5 mmol/L, and glucose concentrations 7.9 mmol/L.

Over the 30 min after return of spontaneous circulation, the remaining 350 mL contained in the Intralipid bag were infused. During this time, his heart rate and rhythm reverted to sinus tachycardia at 110 bpm. The circulation was supported with an epinephrine infusion that was progressively decreased to 0.06 $\mu g \cdot kg^{-1} \cdot min^{-1}$ at this time.

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Accepted for publication November 24, 2008.

Reprints will not be available from the author.

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DOI: 10.1213/ane.0b013e3181979e17

The patient remained hemodynamically stable and, at the end of this 30 min period, it was decided by the anesthesiologist and surgeon to proceed with the planned debridement. This was facilitated by administering a 5 mg bolus of midazolam and isoflurane (end-tidal partial pressure 0.5 kPa). The debridement was completed within 10 min.

After surgery, the patient remained in the operating room until intensive care unit admission was possible. However, at the end of the next 30 min period, (approximately 40 min after the conclusion of Intralipid infusion), a progressively accelerating sinus tachycardia at a rate of 140 bpm, accompanied with frequent multifocal ventricular extrasystoles and short, self-terminating runs of ventricular tachycardia were observed. In view of what was presumed to be the recurrence of bupivacaine cardiotoxicity, additional Intralipid was ordered. However, the recovery room's emergency stock was comprised of only one 500 mL bag which had now been used and no additional Intralipid could be obtained for several hours. Therefore, an amiodarone initial loading dose of 300 mg in 200 mL of 5% dextrose was infused over 30 min.

Admission to the intensive care unit took place 1 h after completion of the amiodarone loading dose by which time the arrhythmias had terminated and inotropic support was discontinued. The patient was tracheally extubated 5 h after his initial episode of systemic toxicity. Despite an initial serum amylase concentration of 608 IU/L, no clinical signs of pancreatitis were noted. On the first postarrest day, total creatine kinase of 2378 IU/L, MB fraction 26 μg/L and Troponin I 1.255 μg/L suggested that myocardial damage had occurred. Four days later, cardiac enzyme levels decreased to 765 IU/L, 1.1 μg/L and 0.059 μg/L, respectively. Hospital discharge occurred 4 days after the initial event.

DISCUSSION

The outstanding feature of this case was the recurrence of cardiovascular instability 40 min after completion of Intralipid administration for bupivacaine cardiotoxicity. We attributed the cardiovascular instability to recurrence of local anesthetic toxicity after lipid rescue, a scenario not previously described. The cause of recurrence of toxicity was likely multifactorial. The serum concentration of Intralipid would have decreased due to redistribution and metabolism. The elimination half-life of IV bupivacaine is longer than all other currently used local anesthetics, reportedly 3.5 h.[17] This may have been prolonged because of poor hepatic function and perfusion in the aftermath of the cardiac arrest. Bupivacaine may have redistributed back into the central compartment. Initial tissue entry and subsequent acidosis-related ion trapping,[17] with later release into the plasma as the acidosis resolved, would have increased the plasma concentrations of bupivacaine. Furthermore, pulmonary uptake of local anesthetics decreases arterial concentrations by 20%; subsequent release of local anesthetic occurs over an unknown time, in an exponentially decreasing manner.[18]

For treatment of local anesthetic toxicity, both the Association of Anesthetists of Great Britain and Ireland (AAGBI)[19] and Weinberg[20–22] currently recommend an initial bolus of 1.5 mL/kg of 20% lipid emulsion administered over 1 min. This bolus may be repeated twice at 5 min intervals if an adequate circulation has not been restored. The bolus should be followed by an infusion of 0.25 to 0.5 mL $\cdot$ kg^{-1} $\cdot$ min^{-1}, the AAGBI recommending administration over 20 min, whereas Weinberg recommends the infusion be continued for 30 min. Weinberg suggests that a total dose exceeding 8 mL/kg 20% lipid emulsion is not likely to be needed.[21,22] These recommendations imply that a single 500 mL bag will suffice for most 60–70 kg patients. However, our case lends support to the AAGBI recommendation that at least 1000 mL 20% lipid emulsion should be available.[23,24]

The postoperative increase in serum amylase could indicate pancreatic injury. While pancreatitis is a known complication of chronic hyperlipidemia,[25] the significance of the hyperamylasemia seen in our patient is currently unclear. Although we cannot find another documented increase in amylase or pancreatic injury after the use of lipid emulsion in resuscitation, this issue must be considered after lipid rescue.

In summary, we report a case of recurrent systemic local anesthetic toxicity after successful treatment with lipid emulsion. Because no additional lipid emulsion was available, the recurrent dysrhythmias were treated with amiodarone. This case documents the importance of the availability of a sufficient quantity of lipid emulsion when regional anesthesia is performed.

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