Severe local anesthetic toxicity is potentially life threatening and is often refractory to standard resuscitative measures. Infants are a particularly susceptible population in this regard because of their unique physiologic features. Recently, 20% intravenous (IV) lipid emulsion (Intralipid) has been proposed as a “one-stop solution” to toxicity related to all commonly used amide local anesthetics. There is an abundance of literature describing its uses in association with regional blocks in adults. However, there is a scarcity of reports describing its application in children, and use of 10% IV lipid emulsion (Intralipid) has not been described in children for rescue therapy, to our knowledge. We report a case of accidental life-threatening overdose of IV lidocaine (lignocaine) in an infant, which was successfully managed with 10% lipid emulsion.

Keywords: Anesthetic overdose, complication, infant, intravenous lipid emulsion, local anesthetic.

Since its introduction in anesthesia practice as an antidote to local anesthetic systemic toxicity (LAST), intravenous lipid emulsion (IVLE) has documented a remarkable success and safety record. The medical literature is now replete with case reports of its use, mostly in adult patients, during regional anesthesia.1-6 However, there is a dearth of clinical reports of the application of IVLE in the pediatric population in general and infants in particular. The clinical use of 10% IVLE (Intralipid) in relation to local anesthetic (LA) toxicity has not been reported to date, to our knowledge. We are reporting a case of massive accidental intravenous lidocaine (lignocaine) intoxication (10 times the recommended dose) in an infant with arthrogryposis multiplex congenita, where early use of 10% IVLE prevented the deterioration of the clinical condition and any adverse sequela.

Case Summary
A 3-month-old male infant, weighing 3.9 kg, with a diagnosis of arthrogryposis multiplex congenita with congenital knee dislocation and bilateral talipes equinovalvarus was scheduled for femoral neck shortening and soft-tissue alignment surgery. The patient had an upper respiratory tract infection 2 weeks before surgery, which had been treated. Results of preoperative investigations were within normal limits. He had a potentially difficult airway due to marked retrognathia and high arched palate. Injection of fentanyl (8 µg) was given for premedication. Thereafter, anesthesia was induced with 5% to 8% sevoflurane in 100% oxygen. His trachea was intubated using a 4-mm polyvinyl chloride uncuffed endotracheal tube with a video laryngoscope (Truview PCD, Truphatek International Ltd, Netanya, Israel) and neuromuscular blockade initiated with injection of atracurium, 2 mg. The patient was then positioned in the left lateral position, and caudal block was administered with 3 mL of 0.25% bupivacaine. The intraoperative course of 90 minutes was uneventful.

At the end of surgery, neuromuscular blockade was reversed with injections of neostigmine and glycopyrrolate. Soon thereafter, the patient experienced labored respiration and paradoxical movement of the chest and abdomen, with inspiratory stridor suggestive of laryngospasm. Symptoms were partially relieved with positive pressure ventilation, application of jaw thrust, and injection of 4 mg of propofol. A trainee administered preservative-free lidocaine (Xylocard) intravenously according to the consultant’s advice.

Suddenly we noticed that the baby became unresponsive, and the electrocardiography monitor showed a wide complex rhythm (Figure 1) with a decrease in heart rate (from 180/min to 102-124/min) and blood pressure (from 67/44 mm Hg to 41/18 mm Hg). Bag-mask ventilation was initiated, and 50-mL bolus of Ringer’s lactate was administered immediately. Simultaneously, focal seizures were noted in the right upper limb, which initially subsided with intravenous administration of midazolam (0.2 mg) but reappeared as generalized tonic clonic seizure. On inspection, we were shocked to learn that 6
358 mL of lidocaine (20 mg/mL; a total dose of 120 mg) had been injected instead of 6 mg.

Immediately, 10% IVLE (Intralipid, 100-mL bottle, Fresenius Kabi AB, Uppsala, Sweden) was administered at a dosage of 3 mL/kg (12 mL) slowly over 2 to 3 minutes. Within a few minutes of completion of the injection, seizures subsided, and his heart rate (now 168/min) and blood pressure (now 57/39 mm Hg) normalized. However, the baby was still lethargic with low muscular tone. The electrocardiogram, although it had converted to narrow complex sinus rhythm, was still showing ST-segment depression (Figure 2). Hence, a second bolus of 10 mL of 10% lipid emulsion was given, followed by infusion at the rate of 1 mL/min for 2 hours. Five minutes following the second bolus (approximately 30 minutes following the event), ST-segment changes also subsided (Figure 3).

The child was intubated and moved to the intensive care unit (ICU) for overnight ventilation with midazolam sedation. There was no recurrence of seizure in the ICU, his vital signs remained stable, and he was extubated uneventfully next morning. He was discharged 3 days later after confirming normal biochemistry profile, including serum amylase and triglyceride.

**Discussion**

To the best of our knowledge, ours is the first reported case of such massive (120 mg instead of 12 mg) intravenous lidocaine overdose in an infant and the use of 10% lipid emulsion to treat it.

Rosenblatt et al\(^1\) were the first, in 2006, to demonstrate the clinical effectiveness of IVLE for resuscitation in a patient with cardiac arrest resulting from bupivacaine toxicity. Since then, IVLE has been reported for resuscitating patients with all other amide LA (ropivacaine, lidocaine/lignocaine, levobupivacaine, and mepivacaine) toxicities.\(^2\)\(^-\)\(^6\) The impressive success story of IVLE led to its adoption for treatment of LA-induced toxicity by various professional bodies, including the Association of Anaesthetists of Great Britain and Ireland, American Society of Regional Anesthesia and Pain Medicine, and American Heart Association.\(^7\)\(^-\)\(^9\) Most case reports of LA toxicity are related to their use in regional block (where the diagnosis is by exclusion of other causes) and 20% IVLE has been used as an antidote in all the reported cases to date.

Lipid sink, metabolic, and direct inotropic theories have been suggested to explain the mechanism of action of IVLE.\(^10\)\(^-\)\(^12\) Of these, the lipid sink theory is most plausible and suggests that LAs, being lipid soluble, are taken up into this “lipid sink,” reducing their concentration in the aqueous phase, decreasing their unbound fraction, and reducing toxicity.\(^10\) The fact that IVLE has been proved effective in the treatment of other lipid-soluble toxins provides impetus to the theory.\(^13\)
Lipid solubility is defined by an octanol-water partition coefficient (log $P$) of 2 and above. Lidocaine has a log $P$ of 2.39 and is proportionately more lipophilic than mepivacaine and levobupivacaine, suggesting that IVLE should be effective in treating its systemic toxicity.\(^\text{14,15}\)

Dix et al\(^\text{3}\) reported a case of lidocaine toxicity in an adult who had received lidocaine as an antiarrhythmic for ventricular tachycardia. They demonstrated a marked reduction in serum lidocaine levels from toxic levels of 7.6 µg/mL to therapeutic levels of 3 µg/mL 55 minutes after treatment with IVLE. They successfully resuscitated the patient with the use of IVLE after an hour of conventional advanced cardiac life support treatment. Similarly, a 31-year-old male patient with advanced renal disease received an iatrogenic overdose of 1,600 mg of 2% lidocaine by infiltration for replacement of a peritoneal dialysis catheter. Features of severe central nervous system toxicity developed, which were successfully and dramatically reverted with a single 1.5 mL/kg intravenous bolus of IVLE.\(^\text{16}\) A recent in vitro analysis of the effects of IVLE on LA concentrations in human blood documented a significant reduction in lidocaine levels after 10% and 20% IVLE treatment.\(^\text{17}\) Another in vitro study reported that IVLE mediated reversal of bupivacaine, ropivacaine, and lidocaine-induced vasodilation in a rat aorta model.\(^\text{13}\)

Lidocaine has a prolonged elimination half-life, increased volume of distribution, and reduced serum binding proteins in young infants, which increases their vulnerability to LAST. Lidocaine-induced seizure has been reported previously in neonates and infants and it is a relatively short-acting amide LA, and in cases of mild toxicity, initial symptomatic management should suffice in most cases. However, severe systemic toxicity is considered an emergent situation and can lead to cardiac arrest with fatal consequences. In our patient, IVLE bolus and infusion proved invaluable because it helped bring serum levels below the toxic range and “buy” time for metabolic pathways to eliminate the drug from the body.

Earlier, IVLE was used after ongoing resuscitative measures failed and when hypoxia, acidosis, and electrolyte abnormalities had already set in. In these conditions, IVLE may be ineffective because of lowered binding affinity to the LA molecule.\(^\text{19}\) Also, a high dose of epinephrine used for resuscitation may further reduce its efficacy.\(^\text{20}\) Hence, there has been a recent trend of early rather than late use of IVLE during suspected LAST.\(^\text{5,6}\) The latest guidelines of the American Society of Regional Anesthesia and Pain Medicine also recommend the use of IVLE at the first sign of toxicity after airway management.\(^\text{9}\)

We did not have 20% lipid emulsion at our facility, and the baby had received 10 times the routine dose of LA intravenously. Imminent danger of cardiovascular collapse and the presence of recurrent seizure pushed us into using 10% IVLE within 5 to 7 minutes of the injection of lidocaine. For treatment of LAST, 20% IVLE has been recommended as an initial bolus of 1.5 mL/kg. Hence, we used a dosage of 3 mL/kg of 10% (12-mL) IVLE as an initial bolus. We presume that the IVLE injection brought the plasma levels of lidocaine below the toxic range and led to immediate improvement in the clinical picture. Infusion was continued to bring the LA levels below critical levels so that there was no recurrence of toxicity. Our facility did not have the ability for measurement of serum lidocaine levels to objectively demonstrate any fall in lidocaine levels after IVLE. However, drawing analogy from a previous case report and keeping the temporal association of events in mind, the favorable outcome in our case was presumably due to IVLE itself. In our case we had used 142 mL of 10% IVLE in total, which is well below the maximum recommended dose (maximum dose of 40 mL/kg over 24 hours, 160 mL for our patient).\(^\text{21}\)

Wong et al\(^\text{22}\) reported the use of IVLE in a 6-year-old, 24-kg child for treatment of bupivacaine-induced cardiac arrest. They administered a 20-mL bolus of 20% IVLE (Intralipid) to the child to a total dose of 190 mL. They demonstrated a reduction in serum bupivacaine levels after IVLE administration and could taper off vasopressors after its use. Shah et al\(^\text{23}\) gave an account of LAST in a 40-day-old, 5-kg infant after caudal block with bupivacaine (10 mg). A 10-mL dose of 20% lipid emulsion was given as a single bolus over 1 to 2 minutes approximately 5 minutes after the bupivacaine injection, following which the baby had clinical improvement and an uneventful recovery. Laboratory test results and 1-week follow-up of the infant did not reveal any adverse effects.

Immediate recognition of the toxicity, continuity of care, and early use of IVLE possibly led to the favorable outcome in our patient. We therefore would advocate early use of IVLE in suspected or proven cases of LAST in infants and children. We also suggest the use of 10% IVLE in cases in which for logistic reasons 20% lipid emulsion cannot be made immediately available. It remains to be determined which preparation and concentration of IVLE is most effective and safest in this high-risk population.

REFERENCES
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