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Use of Intralipid in an infant with impending cardiovascular collapse due to local anesthetic toxicity

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Abstract
Local anesthetic-associated cardiac toxicity following caudal epidural blockade is, fortunately, a rare event. Prompt recognition and early treatment is the key to successful resuscitation. Early use of the lipid emulsion Intralipid in bupivacaine-induced cardiac toxicity may lead to a good outcome.

Key words Intralipid · Bupivacaine toxicity · Caudal block

Introduction

We present the first reported case of the use of 20% Intralipid (Baxter Healthcare, Deerfield, IL, USA) lipid emulsion in an infant with impending cardiovascular collapse due to local anesthetic toxicity following caudal epidural blockade.

Case report

A 40-day-old 4.96-kg baby boy was scheduled for a right inguinal hernia repair under general anesthesia. Past medical history revealed a baby born at full term with complaints of intermittent vomiting and diarrhea since birth. He was not on any medications and had a 24-gauge intravenous access in his right upper extremity. His vital signs in the preoperative holding area included pulse rate of 120 beats·min^{-1}, blood pressure of 75/35 mm Hg, and oxygen saturation of 99% on room air.

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After the placement of standard American Society of Anesthesiologists (ASA) monitors in the operating room, anesthesia was induced with intravenous glycopyrrolate 50 μg, propofol 20 mg, and rocuronium 3 mg. The trachea was intubated with a 3.5-mm internal diameter (ID) uncuffed endotracheal tube. Following uneventful induction, anesthesia was maintained with 40% oxygen, 60% nitrous oxide, and 2% sevoflurane. The baby was then turned to the left lateral decubitus position for the placement of a caudal epidural block. The sacral hiatus was identified and the caudal epidural space was located with a 22-gauge short bevel needle. After negative aspiration for blood and cerebrospinal fluid, 0.5 ml of 0.25% bupivacaine with epinephrine 1:200000 was injected as a test dose. Following a negative test dose, the remaining volume of 3.5 ml of 0.25% bupivacaine with epinephrine was injected in incremental doses over 2–3 min. Immediately following completion of the injection of the local anesthetic, the heart rate (HR) increased from a baseline of 140 beats·min^{-1} to 170 beats·min^{-1}. The ST segment was noted to be elevated 2–3 mm and the T-wave was inverted. The oxygen saturation decreased to 80%, the end-tidal carbon dioxide concentration decreased to approximately 20 mmHg, and the blood pressure decreased to 31/19 mmHg. The baby was turned to the supine position, the inhalational anesthetic was turned off, and the patient was ventilated with 100% oxygen. Epinephrine 2 μg·kg^{-1} and 20 ml of 5% albumin were given intravenously. The oxygen saturation improved to 100%, but the EKG changes persisted. Epinephrine 2 μg·kg^{-1} was repeated with no effect. Suspecting local anesthetic toxicity, 10 ml of 20% Intralipid (Baxter Healthcare; approximately 2 ml·kg^{-1}) was given intravenously over 1–2 min approximately 5 min after the initial event. The patient's hemodynamics stabilized and the EKG tracing reverted back to baseline over the next few minutes. An infusion of Intralipid was ordered, but not started, because there were no further changes in the vital signs

or the EKG tracing. Anesthesia was resumed with oxygen, nitrous oxide, and 2% sevoflurane and the patient was monitored closely. After an uneventful observation period of 15 min, the surgery commenced. Fentanyl 10 μg was given intravenously for analgesia based on increased HR and blood pressure with the surgical stimulus The remainder of the surgical course was smooth and at the completion of surgery, the baby was awakened and the trachea extubated. The failure of the caudal block was further evidenced by the absence of motor blockade and withdrawal response to painful stimuli in the recovery room.

The patient was observed in the intensive care unit overnight and had no further problems. He was discharged home the next day in a stable condition.

Discussion

In children anesthetized with epidural anesthesia, unintentional intravascular administration of the local anesthetic occurs in fewer than 1% of cases [1]. Current suggested criteria for a positive test dose in anesthetized children include HR increase of more than 10 beats·min^{-1}, systolic blood pressure increase of more than 15 mmHg, and an increase in T-wave amplitude of more than 25% in lead II. T-wave changes could be due to either epinephrine or bupivacaine or a combination of the two drugs [2]. It has been reported that accidental intravascular injection can occur after a negative aspiration test for blood in caudal epidural blocks [3,4]. Incremental injection of local anesthetic while closely monitoring the EKG and the vital signs has been recommended to prevent local anesthetic toxicity due to inadvertent systemic injection. In fact, in his review article on local anesthetic toxicity, Tobias [2] suggested that the test dose should be administered incrementally in 0.1- to 0.2-ml·kg^{-1} aliquots with an observation time of 60–90 s after each injection. However, as pointed out by Baum [5], this would require taking up to 10 min for injecting the total local anesthetic dose and may not be practical in most clinical scenarios.

Bupivacaine has been widely used for years and is still the most popular local anesthetic for caudal epidural blockade in children [6]. Cardiac arrest resistant to resuscitation following systemic toxicity and a prolonged effect on the cardiac conduction system are drawbacks of bupivacaine [7]. Toxic doses of bupivacaine markedly suppress cardiac contractile performance and can induce arrhythmia and cardiac arrest in humans [8]. Infants are at greater risk of bupivacaine toxicity because the level of [alpha] 1-acid glycoprotein, which binds with bupivacaine, is decreased in infants compared with levels in older age groups [9]. The recommended safe dose of bupivacaine for caudal epidural blockade in infants is 2.5 mg·kg^{-1} [10]. Newer local anesthetic agents such as levobupivacaine and ropivacaine may provide comparable caudal analgesia with reduced cardiac and central nervous system toxicity [6]. However, since 2004 levobupivacaine has not been available in the United States. Ropivacaine, in contrast to bupivacaine, has local vasoconstricting properties and is not available premixed with epinepherine in commercially available injections. There are conflicting reports regarding the advisability and the effectiveness of adding epinepherine to ropivacaine for epidural injection [11,12]. Ropivacaine may be a less cardiotoxic option; however, using ropivacaine without epinepherine for regional blockade undermines hemodynamic criteria as one of the early warning signs of intravascular injection [13]. Intralipid (Baxter Healthcare) is a sterile, nonpyrogenic fat emulsion prepared for intravenous administration as a source of calories and essential fatty acids. It is made up of soybean oil, egg yolk phospholipids, glycerin, and water for injection. In the serum, it forms small lipid droplets with a diameter of less than 1 micron. The formation of fat emboli is a concern with lipid emulsion administration, but these emboli are generally associated with fat droplets larger than 1 micron, and have not been reported in any cases of Intralipid use for local anesthetic toxicity [14]. Other immediate concerns with Intralipid administration include allergic reactions and thrombophlebitis. Delayed reactions such as splenomegaly, altered liver function, pulmonary hypertension, and thrombocytopenia are not much of a concern with the acute, short-term administration of the lipid emulsion [15].

The exact mechanism underlying the lipid emulsion reversal of local anesthetic toxicity is unclear. It is proposed that bupivacaine partitions preferentially into lipid globules and a "lipid sink," creating decreasing cardiac bupivacaine concentrations after lipid infusion [16]. Another alternative theory is a possible positive metabolic effect of lipid infusion [17]. It has been suggested that local anesthetics inhibit mitochondrial carnitine-acylcarnitine translocase, and elevated triglyceride levels provide an important energy source for the myocardium [18]. Weinberg et al. [19] recommend a dose of 1 ml·kg^{-1} bolus of 20% lipid emulsion for local anesthetic-associated cardiac arrest and starting an infusion of 0.25 ml·kg^{-1}·min^{-1} for 10 min, while continuing cardiopulmonary resuscitation (CPR). The bolus dose could be repeated every 5 min if needed, about two to three times. The Association of Anaesthetists of Great Britain and Ireland recommend a bolus dose of 1.5 ml·kg^{-1} over 1 min of 20% Intralipid, followed by an infusion of 0.25–0.5 ml·kg^{-1} min until the patient is stabilized. The rapid appearance of the cardiovascular depressant effect of the local anesthetic agent in our patient likely points to an intravascular

or intraosseous injection rather than rapid absorption as the probable cause. It is possible that partial intravascular injection may have contributed to the lesser severity of the symptoms as opposed to complete cardiovascular collapse. It is also likely that the prompt use of Intralipid prevented this scenario. Differential diagnoses of cardiac arrest-like hypoxia, anesthetic overdose, anaphylactic reaction, and pneumothorax were considered, but these were thought unlikely due to the absence of other clinical signs and the timeline of events. Blood levels of bupivacaine would have helped confirm the diagnosis, but unfortunately, blood samples were not drawn. Cardiopulmonary resuscitation in local anesthetic toxicity should always begin with the ABC: airway, breathing, and cardiovascular support. However, in cases with high index of suspicion of local anesthetic toxicity due to inadvertent systemic injection, we highly recommend the early use of a lipid emulsion such as Intralipid.

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