Case Report: Misdiagnosed local anesthetic toxicity: a review of the pharmacokinetics and dosing of bupivacaine

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Introduction:
The use of epidural blockade for postoperative analgesia in pediatric patients has become an increasingly valuable practice in perioperative care. While local anesthetics are often at the core of neuroaxial techniques, they have a relatively modest therapeutic index and there may be significant morbidity associated with toxic doses. The pharmacokinetic properties and dosing of bupivacaine (Figure 1) differ between adult and pediatric patients and an understanding of these differences is critical.

We report the use of a continuous epidural infusion that was thought to have precipitated a tonic-clonic seizure in an eight-year-old female. We also review the literature on the pharmacology of bupivacaine.

Case Report:
An eight-year-old (20.5kg) female with a history of ulcerative colitis presented for an open ileostomy closure and ileoanal pull-through. After induction, a mid-thoracic epidural was placed. Aspiration was negative for cerebrospinal fluid and blood. A test dose of 3mL of bupivacaine 0.125% with 1:20,000 epinephrine precipitated no change in heart rate. She was later given an epidural bolus of 8mL of bupivacaine 0.25%. Bupivacaine 0.1% with hydromorphone 20mcg/mL was started at an infusion rate of 6ml/hr. To maintain hemodynamic stability, the infusion rate was decreased in stepwise fashion to 3ml/hr.

In the post-anesthesia care unit, the infusate was changed to bupivacaine 0.1% at 4ml/hr. Overnight, she endorsed increased pain and 2.5ml of bupivacaine 0.1% was bolused and the infusion rate was increased to 5ml/hr.

During morning lab draw, she became unresponsive and had tonic-clonic movements. She was immediately treated with intravenous lorazepam. For detailed timeline, see Figure 2.

A bupivacaine level was drawn one hour after the episode. An EEG demonstrated intermittent focal slowing over the right posterior temporal region. Her event was thought to be a provoked seizure in the setting of local anesthetic toxicity. The rest of her hospital course was unremarkable.

Two weeks after discharge, her bupivacaine level was 0.4mcg/mL. At 6-week follow-up, she had no long-term sequelae and denied additional seizure activity.

Discussion:
Local anesthetic toxicity manifested by seizures has been reported in pediatric patients with bupivacaine levels as low as 5.6mcg/mL. The elimination half-life of bupivacaine, assuming a steady-state serum concentration, is 4.6±0.5 hours. The maximum infusion rate for children ≥6-months of age is 0.4-0.5mcg/kg/hr.

Given the cited elimination half-life of bupivacaine, the bupivacaine lab value from one hour after the event, and the patient’s infusion rate prior to the event, it is improbable that the event was due to bupivacaine toxicity. The patient’s maximum infusion rate would be 10.25 mL/hr of bupivacaine 0.1%.

We suspect the etiology to be vasovagal syncope related to the phlebotomy at the time of the episode. Vasovagal syncope in children can often manifest as seizures and is often misdiagnosed as epilepsy.

Knowledge of bupivacaine dosing and pharmacokinetics is vital for the pediatric anesthesiologist in diagnosing local anesthetic toxicity.

Key Learning Points:
1. Bupivacaine is one of the most commonly administered local anesthetics for routine intraoperative and postoperative analgesia in children.
2. Toxicities in children (<18-months of age) may occur at lower doses compared with adults due to decreased protein binding of the local anesthetic agent.
3. The maximum recommended infusion rate of bupivacaine for children ≥6-months of age is 0.4-0.5mcg/kg/hr.
4. Agitation, restlessnes, and/or myoclonic movements indicative of CNS excitement secondary to vasovagal syncope may easily be confused for local anesthetic toxicity.

References: