

Brief Communication

Perioperative Pain Management in a Patient with Anaphylaxis to Full Mu-agonists Presenting for Head and Neck Salvage Surgery

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Anaphylaxis during the perioperative period is one of the most feared complications for anesthesiologists who care for surgical patients. While muscle relaxants account for the majority of perioperative anaphylactic reactions, opioids are a rare, yet known, cause for anaphylaxis with a perioperative incidence of 1.4% (1). We present the management of a patient with documented anaphylaxis to phenanthrene derivatives (hydromorphone, morphine, oxycodone, hydrocodone), phenylheptylamine derivatives (methadone), and phenylpiperidine derivatives (fentanyl, alfentanil, remifentanyl, sufentanyl, meperidine).

A 56 year-old ASA class III male presented to the pain management clinic for evaluation and treatment recommendations for his upcoming head and neck salvage surgery. He had a past medical history significant for laryngeal carcinoma status-post radiation therapy, radiation-related pharyngocutaneous fistula, tracheostomy, and multiple documented allergies to opioids. Prior to presenting to our institution, he was previously administered morphine, fentanyl, hydrocodone, oxycodone, hydromorphone, and methadone. These medications all independently resulted in allergic reactions associated with angioedema. He was ultimately referred to Allergy & Immunology for sensitivity testing to various opioid classes including phenanthrenes, phenylheptylamines, and phenylpiperidine derivatives. However, since opioids cause direct mast cell degranulation, it was determined by the allergist that skin sensitivity testing was not recommended. She was unable to determine an opioid that could be used peri-operatively for pain management besides tramadol; he was able to tolerate tramadol without any allergic symptoms. Given his extensive allergy list and upcoming surgery, it was decided that the safest option would be to combine neuraxial anesthesia with non-opioid adjuncts. A previously documented study by Merquiol et al (2) demonstrated the use of cervical epidural anesthesia for laryngeal and hypopharyngeal cancer surgery. In their single-center retrospective cohort study, perioperative cervical epidural analgesia was associated with significantly increased cancer-free survival as compared with patients treated with general anesthesia alone (2). For our patient, our goals were to utilize fluoroscopically guided cervical epidural analgesia to manage his pain perioperatively given his significant allergy history to multiple parenteral and enteral opioids.

After written consent was obtained, the patient was placed in the prone position on the fluoroscopy table. Standard ASA monitors were applied and a peripheral intravenous line was placed. The upper back was prepped with chlorhexidine gluconate and draped in the usual sterile fashion. Initially, fluo-

roscopic anterior-posterior views were obtained of the T1-T2 interspace. The skin and subcutaneous tissues overlying this were anesthetized with bicarbonated 1% lidocaine through a 27-gauge 1.25-inch needle. Then, using an 18-gauge Tuohy epidural needle, we advanced in a coaxial fashion until the ligamentum flavum was engaged. A loss-of-resistance syringe filled with air was applied and a firm loss of resistance was noted at 6 cm. After negative aspiration was confirmed, a Pajunk catheter (Sonolong Nanoline Kit, Pajunk, Geisingen, Germany, 521185-31C) with a radiopaque stylet was threaded under fluoroscopic guidance until the tip was located at the inferior border of C6. After negative aspiration, 1 mL of omnipaque was injected to confirm proper epidural catheter placement on an anterior-posterior as well as lateral fluoroscopic view. The needle was withdrawn and the catheter was secured to the skin. A sterile cap was placed on the epidural catheter. Due to the several allergies to Tegaderm and certain types of adhesive, we confirmed that Hypafix would be safe for catheter securement. A Stat-Lock and Hypafix with a series of 1/4" steri-strips were used to secure the epidural catheter. It was draped over his left shoulder. A test dose consisting of 3 mL of 1.5% lidocaine with 1:200,000 epinephrine was injected to ensure that there was no vascular or intrathecal spread. After 15 minutes, we checked the dermatomal blockade with pin prick testing which demonstrated bilateral dermatomal blockade from C4 to T2 without any respiratory compromise. The patient was advised not to contaminate the epidural site, not to take a shower, or to inject anything through the epidural catheter. He was then discharged from the clinic to home.

The following day, the patient underwent laryngopharyngectomy with tubed left anterolateral thigh free flap, anastomosis to the internal mammary artery in his right chest, right pectoralis flap, and split-thickness skin-graft from the left thigh over the pectoralis flap. After discussions with the surgeons, preoperatively he received the following medication through his percutaneous endoscopic gastrostomy (PEG): gabapentin 1,200 mg, acetaminophen 1,000 mg, and diclofenac 100 mg. Intra-operatively he was started on intravenous ketamine 2 mcg/kg/min and his cervical epidural infusion of ropivacaine 0.1% was started at 6 mL/hour without a bolus. Acetaminophen was continued with 1,000 mg IV every 6 hours and ketorolac 15 mg IV every 6 hours for the first 48 hours. Postoperatively his pain was controlled with an IV ketamine infusion at 2 mcg/kg/min,

acetaminophen 1,000 mg was given via the PEG every 6 hours, diclofenac 50 mg given via the PEG every 8 hours, gabapentin 1,200 mg given via the PEG every 8 hours, and a cervical epidural infusion of ropivacaine 0.1% at 6 mL up to 9 mL per hour without any demand dose. Tramadol 100 mg was given via the PEG every 6 hours as needed for moderate to severe pain. His pain scores ranged from 0 to 6 postoperatively and his cervical epidural catheter was eventually removed on postoperative day 9. The remainder of his postoperative course was uneventful and he was eventually discharged from the hospital.

Discussion

Patients presenting with opioid allergies pose a particular challenge to the anesthesiologist. During the preoperative visit, it is imperative to determine the exact nature of the reaction and what workup has been performed to confirm which medications are safe and which produce cross-reactivity. During cross-reactivity, medications such as opioids may have similar epitopes such that known anaphylaxis to one opioid may trigger anaphylactic/anaphylactoid reactions to other opioids with similar structures (3). Opioids induce direct mast cell degranulation and histamine release, making skin sensitivity testing extremely difficult. Additionally, mast cell degranulation is different depending on the mast cell anatomical location. Skin mast cells have been shown to release histamine while mast cells located in other organs of the body show little to no degranulation when exposed to opioids (4,5).

In our case, the patient presented with known anaphylaxis to the following classes of opioids: phenanthrenes, phenylpiperidines, and phenylheptylamines (6). He did not have any known clinical reactions to morphinans or benzomorphans. It was suggested that all opioids were potentially capable of an adverse reaction and testing was inaccurate because of cutaneous mast cell degranulation associated with all opioids. Based on his previous experience, he was able to utilize tramadol without adverse effect. Tramadol is unique in that it is an atypical opioid with partial mu agonist activity in addition to central GABAergic, serotonergic, and noradrenergic activity (6). For our patient, his perioperative pain management plan involved a multimodal approach with sub anesthetic doses of ketamine (Glutamate N-methyl-D-Aspartate receptor antagonist), acetaminophen, diclofenac/ketorolac (cyclooxygenase inhibitors), and gabapentin. This was combined with continuous cervical epidural analgesia with local anes-

thetic, sodium-channel blockade, only. Given the extent and nature of the surgery, we anticipated that his pain would not have been adequately treated with only tramadol and intravenous non-opioid analgesics. Tramadol at doses up to 400 milligrams/day provided suboptimal pain control. While it may be difficult to determine the relative efficacy and contribution of the cervical epidural infusion compared with other components of the multi-modal analgesic regimen, the patient noted significant benefit from the epidural infusion.

For these difficult patients, pain physicians are optimally positioned to assist in the perioperative management of their pain. The use of fluoroscopy allows the safe placement of cervical epidural catheters as well as ensuring the optimal position of the catheter such that the appropriate dermatomal segments will be anesthetized. In this case our test dose of 3 mL of lidocaine 1.5% produced a 7 level dermatomal blockade, which one might not normally expect. Without fluoroscopic confirmation of epidural placement, the anesthesiologist might attribute this finding to intrathecal placement. We hypothesize that this happened in our case due to undiagnosed spinal canal stenosis at multiple levels making this patient's epidural volume smaller, as well as the heterogenous nature (fat and blood vessels) of the epidural space that can result in quite variable dermatomal spread. It is possible that the rate of injection may have also interacted with the above variables

as well. This unexpected result perhaps best exemplifies the value of fluoroscopic guidance to confirm proper epidural catheter placement.

Conclusion

Patients presenting with opioid allergies from multiple opioid classes present a unique challenge to anesthesiologists. Opioids cause direct mast cell degranulation and histamine release independent of the opioid receptor or IgE specific antibodies. Combining neuraxial or regional anesthesia with multimodal non-opioid regimens is an alternative option to improve pain control not only during surgery but also postoperatively. Pain physicians are in a unique position to assist in both the preoperative evaluation as well as the perioperative pain management of patients in whom optimal pain control may be difficult. The use of fluoroscopy for preoperative placement of difficult epidural catheters ensures not only epidural placement but also optimal positioning of the catheter to ensure the appropriate dermatomal segments are covered.

Disclosure

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