Chloroprocaine for epidural anesthesia in infants and children

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The authors discuss their experience with chloroprocaine for epidural anesthesia in five pediatric patients. While bupivacaine remains the most commonly used local anesthetic in children, recent reports of toxicity document the risks of this agent. The major advantage of chloroprocaine is its rapid metabolism, which thereby minimizes the risks of toxicity, especially in patients with preexisting problems such as young age or underlying hepatic dysfunction, which may limit the metabolism of local anesthetics of the amide class.

In three cases, the epidural infusion was combined with the general anesthetic. The cases included hepatic resection, repair of bladder extrophy, and correction of duodenal atresia.

In two other cases, epidural anesthesia was used instead of general anesthesia in a former preterm infant who was undergoing inguinal herniorrhaphy and for lower extremity orthopedic procedures in a child with myotonic dystrophy.

In all cases, chloroprocaine was chosen because of preexisting or associated conditions that might increase the risk of bupivacaine toxicity, such as hepatic resection, repeated dosing in a neonate, or the need for higher concentrations of local anesthetic to achieve adequate surgical conditions. Adequate intraoperative conditions were achieved in all five patients. No complications related to chloroprocaine epidural anesthesia were noted. This initial experience suggests that chloroprocaine offers an acceptable alternative to bupivacaine for epidural anesthesia in the pediatric population.

Key words: Bupivacaine, chloroprocaine, epidural anesthesia, local anesthetics, pediatric anesthesia.

Introduction

The use of epidural anesthesia continues to increase in infants and children. It can be used for postoperative analgesia, as an alternative to general anesthesia, or as part of a combined technique. While several different local anesthetics can be used, the majority of experience has been with bupivacaine. Bupivacaine is generally chosen because of its longer duration of action following a "single shot" technique and its differential selectivity for sensory as opposed to motor neurons.

Although bupivacaine is generally safe and effective, recent reports document significant adverse effects associated with its use, including seizures and ventricular arrhythmias. Pharmacologic work concerning bupivacaine metabolism suggests that these adverse effects theoretically may be more common in infants due to decreased protein binding and limited hepatic metabolism.
While many techniques utilize a "single shot" for postoperative analgesia, repeated dosing or a continuous infusion is needed to provide prolonged intraoperative anesthesia (> 60-90 minutes). With such techniques, the total dose and therefore the risk of toxicity can increase, especially with an agent such as bupivacaine, which has a longer half-life.

We have found that chloroprocaine offers an alternative to bupivacaine for prolonged intraoperative anesthesia. Our experience is presented, and chloroprocaine is discussed as an alternative to bupivacaine for epidural anesthesia in children.

**Case reports**

- **Patient 1.** A 2½-year-old, 19-kg girl was noted to have hepatomegaly during a routine visit to her pediatrician. A further workup revealed a hepatic mass consistent with hepatoblastoma, and she was scheduled for right hepatic lobectomy. Anesthesia was induced with intravenous (IV) thiopental, and tracheal intubation was facilitated with atracurium. Maintenance anesthesia consisted of isoflurane in air/oxygen. Prior to the start of the surgical procedure, an epidural catheter was placed at the L1-2 interspace, using a 17-gauge Tuohy needle and the loss of resistance technique; inadvertent intravascular placement was ruled out by using a test dose of 2 mL of 1% lidocaine with epinephrine 1:200,000. After the test dose, an initial bolus dose of 10 mL of 3% chloroprocaine was administered, followed by a continuous infusion of 1 mL/kg/hr. There was no hemodynamic response to surgical incision with isoflurane (expired concentration, 0.4%). A continuous infusion was maintained at 10 mL/hr throughout the 4-hour surgical procedure. Maintenance anesthesia consisted of isoflurane (expired concentration, 0.2-0.4%), and muscle relaxation was achieved with intermittent doses of atracurium.

Following the surgical procedure, the chloroprocaine infusion was discontinued, and residual neuromuscular blockade was reversed. The patient's trachea was extubated, and she was transported to the recovery room. The epidural catheter was left in place for 72 hours, and postoperative analgesia was provided by a continuous epidural infusion of 0.1% of bupivacaine with fentanyl, 3 μg/mL at 6 mL/hr (fentanyl, 1 μg/kg/hr). The patient had an uncomplicated postoperative course.

- **Patient 2.** During a medical trip to Guatemala, Central America, a 6-year-old, 28-kg girl was scheduled for repair of bladder extrophy. Anesthesia was induced with IV propofol, and tracheal intubation was facilitated by a single dose of mivacurium. No other muscle relaxants were administered during the procedure.

Prior to the start of the surgical procedure, an epidural catheter was placed at the L3-4 interspace using a 17-gauge Tuohy needle and the loss of resistance technique; inadvertent intravascular placement was ruled out by using a test dose of 2 mL of 1% lidocaine with epinephrine 1:200,000. After the test dose, an initial bolus dose of 15 mL of 3% chloroprocaine was administered, followed by intermittent bolus doses of 8 mL every 45-60 minutes. Bolus doses were administered at least every hour or sooner if hemodynamic response to surgical manipulation was noted. Maintenance anesthesia consisted of halothane (inspired concentration, 0.3% in 50% nitrous oxide/oxygen). The patient ventilated spontaneously throughout the 6½-hour surgical procedure.

Following the procedure, the trachea was extubated and the child was taken to the recovery room. The epidural catheter was left in place for 48 hours, and postoperative analgesia was provided by intermittent doses of 8-10 mL of 1/8% bupivacaine with epinephrine 1:200,000. The child had an uneventful postoperative course.

- **Patient 3.** A 2-day-old, 3.6-kg male infant was scheduled for repair of duodenal atresia. Anesthesia was induced with IV thiopental, and tracheal intubation was facilitated with vecuronium. Following anesthetic induction, the infant was placed in the lateral decubitus position. After use of a sterile povidone-iodine preparation, a 22-gauge IV catheter was placed through the sacrococcygeal membrane into the epidural space. Following catheter placement, a t-piece that had been flushed with 3% chloroprocaine was attached to the catheter and secured with a transparent bio-occlusive dressing. An initial dose of 1.5 mL/kg of 3% chloroprocaine was followed by a continuous infusion of 1.5 mL/kg/hr.

Maintenance anesthesia consisted of isoflurane (expired concentration, 0.2%) in air/oxygen. No hemodynamic response was noted to the surgical incision or the subsequent procedure. The surgical procedure lasted 2 hours and 20 minutes. After the procedure, residual neuromuscular blockade was reversed, the infant's trachea was extubated, and he was transported to the recovery room. The caudal epidural catheter was dosed with 3.5 mL of 0.125% bupivacaine and removed. The infant had an uneventful postoperative course.

- **Patient 4.** A 20-week-old, 1.9-kg infant was scheduled for a bilateral inguinal herniorrhaphy. Past medical history was significant for premature birth at 29 weeks' gestation and a weight of 1,100 grams. Mechanical ventilation was required for 35 days following birth, and the infant had residual bronchopulmonary dysplasia with an oxygen requirement of 0.2 L/min. Current medications in-
cluded furosemide and hydrochlorothiazide. The oxygen saturation was 92-94% (with supplemental oxygen at 0.3 L/min).

The surgery was considered necessary because 1 week earlier the left-sided hernia had incarcerated and was manually reduced with difficulty. This event was followed by grossly bloody stools for 24 hours. The patient was on nothing by mouth status for 4 hours, and an IV infusion of 10% glucose in 0.45% saline was started. The infant was transported to the operating room, and routine monitors were placed. A caudal epidural catheter was placed using the same technique as in patient 3.

After negative aspiration for blood or cerebrospinal fluid, a total of 1.5 mL/kg of 3% chloroprocaine was administered in 0.5 mL/kg increments. This was followed by a continuous infusion of 3% chloroprocaine (1.5 mL/kg/hr). Within 5 minutes a motor block of the lower extremities was noted. The sensory level, as judged by a gentle pinprick, was T2-4.

The entire procedure, from the initial dose of chloroprocaine to the completion of the surgical procedure, lasted 150 minutes. No sedative or analgesic agents were given to the infant during this time. The infant became momentarily fussy during the dissection and traction on the cord on the right side, so a bolus dose of 3% chloroprocaine (1 mL) was administered. During the remainder of the procedure, the infant was calm and sucked on a pacifier that had been moistened with a 10% glucose solution. Oxygen saturation, heart rate, and blood pressure were unchanged during the procedure. Following the procedure, the chloroprocaine infusion was discontinued, and the infant was transported back to the neonatal intensive care unit and had an uneventful postoperative course.

**Patient 5.** An 11-year-old, 32-kg boy with myotonic dystrophy and mental retardation presented for tendon transfers and surgical correction of orthopedic deformities of the lower extremities. His previous history was negative for earlier surgical procedures. Physical examination revealed micrognathia with limited mouth opening (2 cm).

Because of the possibility of a difficult airway, a regional anesthetic technique was chosen. Following sedation with IV ketamine (in 10-mg increments), a lumbar epidural catheter was placed at the L3-4 interspace. There was no hemodynamic response to the test dose of 2 mL of 1% lidocaine with epinephrine 1:200,000. An initial bolus dose of 15 mL of 3% chloroprocaine was followed by a continuous infusion of 15 mL/hr.

After placement of the block, the patient slept throughout the surgical procedure, which lasted 3 hours. No other IV anesthetic agents were administered. Postoperative analgesia was provided by a continuous infusion of 0.1% bupivacaine with fentanyl, 3 μg/mL at 6 mL/hour. The patient had an uncomplicated postoperative course.

**Discussion**

Several beneficial effects have been ascribed to epidural anesthesia compared to general anesthesia including improved postoperative analgesia, decreased intraoperative blood loss, a decreased incidence of thromboembolic events, earlier hospital discharge, and improvement in the patient's postoperative metabolic status.7,8 Additionally, epidural anesthesia can be used instead of general anesthesia in high-risk neonates.9

Despite such benefits, recent reports document the inherent risks of regional anesthesia, especially in the pediatric population.4,5 Such risks are primarily attributable to local anesthetic toxicity, and they may be increased in infants and children because of the relatively larger per kilogram requirements of local anesthetic agents, decreased hepatic enzyme maturity, and an increased free fraction of local anesthetic due to decreased protein binding.5 While the majority of experience with regional anesthesia in children has been with the local anesthetic bupivacaine, in certain situations the use of alternative agents may be advisable to limit the likelihood of toxicity.

Chloroprocaine is a local anesthetic of the ester class that has been used most often in obstetrical anesthesia practice. It is rapidly hydrolyzed by plasma esterases and has a half-life of less than 60 seconds, even in infants and neonates.

The use of chloroprocaine for pediatric anesthesia was suggested by a recent report of Henderson and associates, in which continuous caudal anesthesia was used for inguinal herniorrhaphy in high-risk neonates.11 Although many of these procedures can be performed under “single shot” spinal or epidural blockade, anticipated or more importantly unanticipated intraoperative difficulties may require a more prolonged anesthetic.

Most reports have used 3-4 mg/kg of bupivacaine, which will provide 60-90 minutes of surgical anesthesia following a single shot technique. Although such doses will not result in toxic serum concentrations following the initial dose, there may be a risk of attaining toxic serum concentrations when repeated doses are needed.12 To avoid the risk of such toxicity, Henderson and associates recommended the use of chloroprocaine.11 Following an initial dose of 2 mL/kg, a continuous infusion was started at 2 mL/kg/hr. Chloroprocaine levels were measured in five of the patients. The level at the
completion of the infusion was zero in four patients and 0.5 mg% in the fifth.

Aside from limiting toxicity, the additional benefits of 3% chloroprocaine are a rapid onset and a complete motor block that is unlike the partial blockade seen with 0.25% bupivacaine. Complete motor blockade is helpful when the regional anesthetic technique is used instead of general anesthesia when movement can interfere with the surgical procedure. Although its duration is brief following a single administration (30-60 minutes), the use of a continuous infusion or repeated dosing allows for an unlimited duration of the surgical anesthesia.

We have also found further applications for chloroprocaine outside of the neonatal population. Epidural anesthesia may also be chosen as an alternative to general anesthesia in the general pediatric population. Certain predisposing genetic or acquired conditions (i.e., myotonic dystrophy in patient 5) may make the conduct of general anesthesia more difficult. Additionally, the preoperative evaluation in this patient revealed a small mandible with limited mouth opening that suggested a difficult airway. In such patients, epidural anesthesia can be used as the primary anesthetic technique.

Outside the neonatal population, 0.25% bupivacaine does not provide dense sensory blockade and is not acceptable as the sole anesthetic agent. However, the use of higher concentrations such as 0.5% bupivacaine or repeated doses are limited due to the risk of toxicity. Such was the case in our fifth patient, in whom epidural anesthesia was chosen as the primary intraoperative technique. Although an initial dose of 0.5-0.7 mL/kg of 0.5% bupivacaine would have produced adequate intraoperative conditions, we were concerned that repeated dosing would be needed for the anticipated 3-4 hour surgical procedure.

Epidural anesthesia can also be used as an adjunct to general anesthesia (patients 1, 2, and 3). The administration of local anesthetics into the epidural space prior to the surgical procedure effectively blunts the postsurgical stress response and also provides preemptive analgesia, thereby limiting the severity of postoperative pain and postoperative opioid requirements. The addition of regional anesthesia also decreases the requirements for general anesthetic agents and may enable earlier extubation. We have found this to be particularly relevant in our neonatal population.

The addition of epidural anesthesia to general anesthesia can also be used to improve intraoperative conditions by providing muscle relaxation without the need for neuromuscular blockers. Although it is less of an issue in the United States, this was particularly relevant for our second patient in Guatemala, because profound muscle relaxation was required for the surgical closure of the bladder extrophy, yet spontaneous ventilation was desired since mechanical ventilation was not available. In that setting, the sensory and motor blockade with 3% chloroprocaine provided muscle relaxation for surgical closure of the defect and limited the halothane requirements to 0.3%, which allowed for spontaneous ventilation.

Aside from the neonatal population, there are other situations that may alter hepatic function and the ability to metabolize local anesthetics of the amide class. Our first patient underwent hepatic resection, and we speculated that this procedure might acutely alter serum bupivacaine levels, especially with repeated dosing. Therefore, we felt that an alternative agent such as chloroprocaine was preferable. Aside from hepatic resection, pharmacologic agents (e.g., propranolol and H₂ antagonists) have been shown to alter hepatic blood flow or function and thereby affect the metabolism of local anesthetics. Decreased bupivacaine metabolism has also been demonstrated during the administration of halothane. In such situations, the use of chloroprocaine may limit the risk of local anesthetic toxicity.

The major disadvantage of chloroprocaine is the development of tachyphylaxis, which limits its utility for prolonged use. Therefore, although it is suitable for repeated dosing during surgical procedures, chloroprocaine has not been shown to be effective by continuous infusion for postoperative analgesia. Of additional concern are the earlier reports of neurotoxicity when chloroprocaine (Chloroprocaine-CE, Astra Pharmaceutical Products, Westborough, Massachusetts) was inadvertently injected into the intrathecal space. While initially thought to be related to the anesthetic itself, later investigation linked the neurotoxicity to the low pH and the preservative sodium metabisulfite. Such problems have not been reported with the newer formulation (Chloroprocaine-MPF, Astra Pharmaceutical Products). However, this preparation is still not recommended for intrathecal administration.

Another issue with chloroprocaine are the reports of back pain which is thought to be the result of tetany in the paraspinus muscles related to the preservative, calcium ethylenediamine tetra-acetic acid (EDTA), in the solution. While we did not notice any obvious problems in our patients, the identification of back pain is difficult in infants and young children. Our series also contains a limited number of cases; therefore, no definite estimate of the incidence of this potential side effect can be made.
In summary, we have presented our experience with chloroprocaine as an alternative to bupivacaine for epidural anesthesia in children. Its major advantage lies in its rapid metabolism, which minimizes the risk of toxicity, especially in patients with preexisting problems such as age or underlying hepatic dysfunction that may limit the metabolism of local anesthetics of the amide class. In addition, 3% chloroprocaine provides both sensory and motor blockade, thereby providing adequate intraoperative surgical anesthesia. While there is limited information concerning dosing in children, we found that in neonates an initial dose of 1.5-2 mL/kg will provide a sensory level of T2-4. In older patients, the dose is dependent on the level of blockade that is desired. We prefer Armitage's formula and suggest the use of 0.5-0.75 mL/kg for lower extremity procedures and 0.75-1.0 mL/kg (maximum initial dose of 20 mL) for lower abdominal procedures. Repeated dosing may be required every 45-60 minutes, or a continuous infusion can be used at an hourly rate equal to the initial bolus dose.

REFERENCES


AUTHORS

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