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Original Contribution

Evaluation of prolonged epidural chloroprocaine for postoperative analgesia in infants

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Abstract

Study Objective: To describe the use and adverse effects of chloroprocaine for epidural analgesia in young infants for infusion durations greater than 3.5 hours.

Design: A retrospective cohort review of the electronic medical record over a 14-month period.

Setting: The level IV neonatal intensive care unit of a 414-bed free-standing children's hospital.

Patients: Eighteen infants (mean age, 1.7 ± 1.8 months [0.03-6.3]; mean weight, 3.8 ± 1.3 kg [1.56-6.9]; n = 10 [55%] males) received 1% chloroprocaine for epidural analgesia postoperatively for up to 96-hour duration and met criteria for inclusion.

Measurements: Dosing requirements, placement of epidural catheter, supplementary analgesic therapy, respiratory support, vital signs, and incidence of adverse events associated with local anesthetics were collected.

Main Results: Epidural catheter placement was caudal (n = 8), lumbar (n = 6), or thoracic (n = 4). Mean operative time was 2.48 ± 1 hour (1-5). Initial chloroprocaine dose was 1.3 ± 0.5 mL/h (0.4-2.5) (3.5 ± 1 mg/kg per hour [1.4-5]) with a maximum dose of 1.5 ± 0.6 mL/h (0.4-3) (4.2 ± 1.1 mg/kg per hour [2.2-6.1]). Duration of epidural analgesia was 48.3 ± 21.5 hours (10-96). Duration of epidural infusion did not influence dosing requirement, suggesting the absence of drug tachyphylaxis. All patients received intermittent doses of opioid and nonopioid pain medications while receiving chloroprocaine. Two mechanically ventilated patients required continuous infusion of opioids. No adverse events were directly attributed to chloroprocaine use.

Conclusion: Epidural 1% chloroprocaine, in doses of 0.4-3 mL/h (1.5-6.1 mg/kg per hour), was well tolerated in both mechanically ventilated and spontaneously breathing infants for up to 96 hours with no identified adverse effects or tachyphylaxis.

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1. Introduction

Chloroprocaine is an aminoester local anesthetic. It was first introduced into clinical practice in the early 1900s, but its use diminished due to associations with allergic reactions and prolonged sensory motor deficits after unintentional subarachnoid injection. Chloroprocaine possesses a low partition coefficient, no protein binding, an extremely fast onset, and an ultrashort duration of action. Unlike other local anesthetics, chloroprocaine has a half-life measured in seconds (compared to hours) and is metabolized by plasma cholinesterase, which does not require the liver for metabolism [1]. These features are advantageous in neonates who have immature hepatic enzymatic systems for drug metabolism and are at higher risk for drug accumulation/toxicity from medications requiring biotransformation in the liver. Although chloroprocaine has been used successfully in neonates for brief (lasting <3.5 hours) operative procedures, descriptions of prolonged, postoperative use have not been published [2,3]. We report our experience with continuous epidural chloroprocaine in neonates and young infants after a number of operative procedures. The specific aims of this study are to describe the dosing regimens of chloroprocaine (starting dose, titration, and duration), the occurrence of adverse effects, and additional analgesic medication requirements for adequate pain control during epidural infusion.

2. Methods

The local institutional review board approved this study, and the requirement for written consent was waived. After institutional review board approval, we retrospectively reviewed the charts of infants (<7 months of age) admitted to our neonatal intensive care unit (NICU) that received epidural chloroprocaine for postoperative analgesia during a 14-month period from June 2012 to August 2013. The NICU is an 82-bed level IV medical and surgical unit, within a freestanding children's hospital. Subjects were identified with the assistance of a clinical information resource specialist using data extracted from our electronic medical record system (Epic Systems, Verona, WI). Patient age, sex, weight, gestational age at birth (weeks), duration and type of surgery, location of epidural catheter, intraoperative anesthetic, and supplementary postoperative analgesics up to 24 hours after discontinuation of the chloroprocaine epidural were analyzed. Documentation of adverse effects reported with chloroprocaine (bradycardia, cardiac arrest, hypotension, ventricular arrhythmias, seizure, edema, respiratory arrest, and allergic reactions/anaphylactoid reactions) was noted. Pain scores, using the Face, Legs, Activity, Cry, Consolability (FLACC) scale or Premature Infant Pain Profile scale (PIPP), were collected for the duration of epidural infusion [4,5]. The initial chloroprocaine dose (milliliters per hour and milligrams per kilogram per hour), maximum dose (milliliters per hour and milligrams per kilogram per hour), duration of infusion (hours), and number of dose titrations were recorded for each patient. Finally, the doses and frequency of acetaminophen (oral, rectal, or intravenous), ibuprofen or ketorolac, dexmedetomidine, or opioids (fentanyl, morphine, oxycodone, or hydromorphone) administered during the chloroprocaine epidural were collected. In an effort to recognize the potential influence of mechanical ventilation on the overall requirement for additional analgesia and sedation, we evaluated patients based on duration of mechanical ventilation. Patients who were extubated and spontaneously breathing within 24 hours of the operative procedure were compared to those who remained on mechanical ventilatory support beyond the 24-hour postoperative period. In addition, patients were divided into clonidine- and non–clonidine-containing epidural groups for evaluation of all outcomes. Quantitative variables are described using measures of central tendency (mean, median, and SD). We report data as mean ± SD (range), unless significant skewness was detected, in which case, data will be stated as median. Qualitative or categorical data are described as frequency and percentage. The Student *t* test and analysis of variance were performed to detect any statistical differences in outcome variables. $P < .05$ was considered statistically significant.

3. Results

A total of 18 patients were enrolled. The mean age was 1.7 ± 1.8 months (0.03-6.3 months), and the mean weight at time of chloroprocaine administration was 3.8 ± 1.3 kg (1.56-6.9 kg). Fifty-five percent of the patients (n = 10) were male. Surgical procedure, duration of operative event, catheter placement, and initial chloroprocaine dose are listed in Table 1. The overall mean operative time was 2.48 ± 1 hour (1-5 hours). The caudal approach to epidural catheter placement with subsequent threading to the thoracic level was most common. Of the 18 epidurals placed, 13 were confirmed by epidurogram, and 2 were confirmed by ultrasound. Ninety-five percent of patients (n = 17) received inhalational anesthesia during their operative event. Most patients (n = 10, 55%) had their continuous epidural initiated intraoperatively. For those subjects who had postoperative epidural initiation, the time to start was 2.86 ± 2.74 hours (0.76-9.37 hours) after surgery. Most patients were quickly extubated after their procedure (n = 10 within 3 hours; n = 3 within 3-24 hours; n = 5 greater than 24 hours after the procedure). Of the 13 patients who were extubated within 24 hours of their procedure, 10 returned to their baseline oxygen requirement, whereas 3 required higher flow or percentage of oxygen. Five patients received mechanical ventilatory support beyond 24 hours of the procedure. The mean time to extubation was 95 ± 79 hours (30-214 hours); 3 of the 5 patients remained on mechanical ventilation after discontinuation of the epidural.