Compounded LOCAL ANESTHETICS to Minimize Pain from Medical Procedures

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ABSTRACT

Medical procedures do not have to be painful. There are several available pharmacologic options, both commercial and compounded, for providing local anesthesia and thus minimizing the fear and stress associated with these procedures. No patient should suffer because the clinician lacks the knowledge or comfort level necessary to provide adequate analgesia during painful medical procedures. Compounding pharmacists can prepare local and topical anesthetics for clinics, emergency departments, patient-care units, and physicians' offices to keep on hand for medical emergencies and procedures; this reduces the waiting period for patients, allows procedures to be performed efficiently, and improves patient care.

Pain is one of the major complaints and fears of patients, regardless of age. Pain is recognized by the Joint Commission on Accreditation of Healthcare Organizations as the fifth vital sign.1 Medical procedures, such as suturing lacerations or inserting peripheral intravenous central catheters, are often painful but necessary in the treatment of patients. The pain associated with these procedures can be stressful for the patient as well as the patient's caregivers or parents and the medical staff. The patient may become uncooperative, requiring physical restraint to complete the medical procedure. Such experiences can be very traumatic for the patient; children who experience a painful procedure may become fearful of all medical personnel, even for routine, painless examinations. Local anesthetics and nonpharmacologic techniques can be used to minimize patient discomfort, reduce stress, and improve patient satisfaction during medical procedures.
Ideally, an anesthetic should (1) be inexpensive, (2) have a rapid onset of action, (3) have a short duration of action, (4) be administered easily, (5) be predictable and effective, and (6) be safe, with minimal adverse effects. This article reviews several compounded topical anesthetics, devices, and nonpharmacologic methods used to minimize procedural pain.

PHARMACOLOGIC STRATEGIES

Buffered Lidocaine

Lidocaine infiltration is the gold standard of care for local anesthesia for repair of lacerations and other medical procedures. It quickly numbs the affected area, and it is inexpensive. Ironically, lidocaine injections are painful because of the acidic pH of the lidocaine solution. Lidocaine has a pKₐ of 7.9 and is commercially sold as a sterile lidocaine hydrochloride injectable solution with a pH as low as 3.82 to improve the shelf life.²,³ Buffering lidocaine with sodium bicarbonate has been shown in studies to reduce the pain of the injection.⁴ Addition of sodium bicarbonate injection to the lidocaine hydrochloride injection raises the pH and effectively increases the concentration of nonionized lidocaine, which is the active form of the drug. Increasing the pH of lidocaine hydrochloride solution from 6 to 7 increases the concentration of nonionized lidocaine from less than 1% to 11%.⁶

Buffered lidocaine may be compounded by a pharmacy for office use, or it can be prepared at bedside before administration, according to the new United States Pharmacopeia (USP) Chapter <797> standards (effective June 2008).⁷ It is typically prepared as a 1:10 solution (1 part sodium bicarbonate 8.4% injectable solution and 9 parts lidocaine hydrochloride 2% injectable solution). There are, however, conflicting reports on the stability and shelf-life of buffered lidocaine. One study reported that the lidocaine concentration decreased from 90% to 80% at 7 days.⁸ Another study reported that buffering a combination of lidocaine and epinephrine reduced the lidocaine concentration to 66% and the epinephrine to 1% of their original concentrations after storage at room temperature for 4 weeks. The same compound stored at 4°C, however, retained 95% of the lidocaine and 82% of the epinephrine.¹ In the November/December 2007 issue of the International Journal of Pharmaceutical Compounding, the stability of buffered lidocaine was reported as 60 days at room temperature.⁹ This beyond-use dating would make it feasible for pharmacies to compound the buffered lidocaine in a sterile environment according to USP Chapter <797> standards. The buffered lidocaine could be dispensed for office use in hospital emergency departments (EDs), patient care units, and clinics. The formulation for buffered lidocaine is included as a sidebar to this article.

Nonpharmacologic interventions can improve the comfort of administration and the efficacy of buffered lidocaine administration. Warming the buffered lidocaine solution to 98°F to 104°F enhances the anesthesia and reduces the pain of the injection.¹⁰,¹¹ Some patients attribute the pain of the lidocaine infiltration to insertion of the needle itself. The J-Tip (National Medical Products Inc, Irvine, California), a new needle-free injection system approved by the U.S. Food and Drug Administration, can be used to administer local anesthetics such as the buffered lidocaine. It is similar to the injections of the future as depicted on the science fiction television show, Star Trek. The J-Tip is a sterile, single-use, needle-less syringe that delivers the medication under high pressure from a compressed carbon dioxide gas cartridge. When activated, the gas drives the plunger down the barrel of the syringe, pushing the medication through a micro-orifice. The medication under pressure penetrates the skin surface and subcutaneous tissues to a depth of 5 to 8 mm. Lidocaine injected by this method was shown by Jimenez et al in a comparison trial with EMLA, a eutectic lidocaine/prilocaine mixture formulated as a topical preparation for local anesthesia, to have a quicker onset of action, to cause no vasodilatation, to provide better anesthetic effectiveness, to decrease the risk of needle-stick injury and the potential for contamination of the sterile solution, and to cost no more.¹²

TAC Solution and Gel

Because of their many advantages, topical anesthetics have become popular for repair of dermal lacerations in children. These advantages include the following:

- Infiltration of the anesthetic causes no tissue distortion.
- Topicals require no painful injection, which makes the treatment much more acceptable to patients and parents and can reduce stress and improve patient cooperation.

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Topical anesthesia reduces the need for physical or chemical restraint and minimizes the potential psychological trauma of the medical procedure. In 1980, Pryor et al published a study comparing a topical solution containing 0.5% tetracaine, 1:2000 epinephrine (adrenaline), and 11.8% cocaine (a solution referred to as TAC) with lidocaine infiltration. TAC was frequently used as a topical anesthetic in children during suturing of uncomplicated lacerations. Although the compounded TAC solution is very effective as a topical anesthetic, its use has diminished with published reports of cocaine toxicity. Systemic absorption of cocaine has been documented by investigators who found cocaine metabolites in the urine and serum of patients receiving TAC. Two deaths in children and seizures have been reported secondary to inadvertent mucosal contact or improper monitoring of the TAC solution.

**Rx**

3% CARBOXYMETHYLCELLOULOSE IN ISOTONIC SALINE STERILE GEL

| Carboxymethylcellulose sodium, medium viscosity | 24 g |
| Methylparaben powder | 2.88 g |
| Propylparaben powder | 0.4 g |
| Sodium chloride 0.9% for injection | q s 100 mL |

**Note:** This formulation should be prepared according to strict aseptic compounding technique in a laminar airflow hood in a cleanroom or via isolation barrier technology by a compounding pharmacist who is validated in aseptic compounding. This is a low-risk preparation.

**Method of Preparation**

1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Weigh and/or measure each ingredient accurately.
3. Heat a portion (approximately 600 mL) of saline solution to dissolve the parabens.
4. Pour heated solution into a blender, add the carboxymethyl cellulose sodium powder, and blend for 30 seconds.
5. Pour mixture into a clean, graduated, autoclavable bottle, and q s to the desired volume with the saline solution.
6. Cap and place bottle in a steam autoclave.
7. Subject to autoclaving on the liquid setting at 15 psi at 250°F for 30 minutes.
8. Remove the autoclaved gel and allow the mixture to cool down until it is very warm to the touch.
9. Pour the gel into a sterile top fill bag, attach tubing from the bag to the peristaltic pump, and pump 60 mL of gel into each 60-mL Luer-lock syringe.
10. Cap syringe with a sterile tamper-resistant cap and label the syringe.

**Stability and Storage**

No stability data are available for this formula. A 180-day beyond-use date is recommended for this formulation since the preparation is chemically stable and preserved.

In a reported 1999 study by Vinci et al, a modified TAC solution was used as a topical anesthetic in suturing lacerations in children younger than 15 years. The modified TAC solution consisted of 0.5% tetracaine, 1:2000 epinephrine, and 5.9% viscous cocaine. A strict protocol was used in the study, and only 25 children were enrolled. Effective anesthesia was achieved and none of the subjects demonstrated any adverse effects suggesting cocaine toxicity. Contraindications to the administration of TAC are as follows:

- History of allergy to any component of TAC or mixtures of lidocaine with tetracaine and epinephrine
- Application on the genitals
- Application intranasally
- Application on distal phalanges
- Application on or in close proximity to a mucosal surface
- Application on the pinna of the ear
- Patient history of heart disease
- Patient history of hypertension
- Patient history of seizures
- Pregnancy

A more recent study by Kennedy et al demonstrated that a topical adrenaline and cocaine gel, also known as topAC, is an effective anesthetic for suturing children’s facial lacerations. The compounded topAC consists of 1:2000 epinephrine and 5% cocaine. No toxic side effects were seen, but the study protocol was updated in line with published evidence. The authors of the study concluded that the gel was less likely to run than TAC, the dose was smaller.

**Rx**

LIDOCAINE HYDROCHLORIDE 1.82% BUFFERED INJECTION

| Lidocaine hydrochloride 2% injection | 100 mL |
| Sodium bicarbonate 8.4% injection | 10 mL |

**Note:** This formulation should be prepared according to strict aseptic compounding technique in a laminar airflow hood in a cleanroom or via isolation barrier technology by a compounding pharmacist who is validated in aseptic compounding. This is a low-risk preparation.

**Method of Preparation**

1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Weigh and/or measure each ingredient accurately.
3. Obtain 100 mL of lidocaine hydrochloride 2% injection.
4. Obtain 10 mL of sodium bicarbonate injection.
5. Mix the two solutions together until uniform.
6. Package and label.

**Stability and Storage**

A beyond-use date of up to 60 days at room temperature may be used for this preparation when a sterility testing program is in place.
but efficacious, and adherence to a safe protocol prevents the disastrous adverse events reported with the original TAC solution. The protocol can be accessed on the Emergency Medicine Journal website at www.emjonline.com/supplemental.

Although TAC and modified versions are very effective local anesthetics, there are other disadvantages to these compounded medications. Since cocaine is a Schedule II drug, the documentation required by the U.S. Drug Enforcement Administration can be tedious for pharmacies. Retail pharmacies may be prohibited from dispensing the cocaine-containing compounds for office use. In hospitals, the cocaine has to be stored in a double vault and be subject to perpetual inventory; inventory records must be kept for 2 years, and inventory records must be monitored regularly. Hospitals must document every dose administered and the amount that is unused and wasted. It can be difficult to get the medical and nursing staff to comply 100% with these regulations, especially during emergency procedures.

Theoretically, the use of TAC could result in tissue hypoxia leading to an increase in wound infections and healing difficulties. One study found that guinea pigs treated with TAC and purposely contaminated with *Staphylococcus aureus* had significantly more infections than those treated with isotonic saline solution alone. Although there is no documentation of increased risk of infection in humans, it can be a concern, especially if the healthcare facility has a large number of immunocompromised patients. TAC is generally not prepared as a sterile compound.

**LET (LAT) Solution and Gel**

A solution or gel containing 4% lidocaine, 0.1% epinephrine, and 0.3% tetracaine (LET), or 4% lidocaine, 0.2% epinephrine, and 1% tetracaine (LAT), offers a less expensive, cocaine-free anesthetic alternative to TAC; the cocaine is replaced with lidocaine. These mixtures originally were tested in 1995 by Schilling et al and shown to be as effective as TAC as topical anesthetics. The gel formulation offers the advantage of adhering to the area to which it is administered and is generally preferred by medical staff. LET gel also can be prepared as a sterile topical compound, reducing the chance of contaminating the wound. The formulation for the 3% carboxymethylcellulose sterile gel base that can be used to prepare the LET gel is included as a sidebar to this article. The gel base is preserved and can be compounded and stored for up to 12 months at room temperature. The formulation for the topical sterile LET gel also is included as a sidebar to this article. It may be compounded, unit-dose packaged in amber topical syringes, and stored in the refrigerator, protected from light, for up to 154 days.

LET gel has a more rapid onset of action than EMLA cream. Maximum anesthesia can take up to 2 hours with EMLA cream, an undesirable wait when suturing a wound or performing other.
medical procedures. LET gel is effective within 20 to 30 minutes of application. A sample protocol of how to administer the LET gel is provided as a sidebar to this article.

Since seizures have been reported in a 20-month-old burn patient treated with 2% lidocaine gel,23 precautions should be taken with LET similar to those taken with TAC (see the precautions in the formulation for lidocaine hydrochloride 1.82% buffered injection that accompanies this article). To date, there have been no serious adverse events reported with the use of LET gel or solution.

NONPHARMACOLOGIC TECHNIQUES

Mary Poppins stated that "a spoonful of sugar helps the medicine go down." There is scientific evidence that sucrose can provide analgesia in newborn infants undergoing painful medical procedures such as injections, lumbar punctures, heel lances, and even circumcision.24 It is postulated that the sucrose activates endogenous opioids in the infants. The taste of the sucrose is foreign to the infant and serves as a distraction, especially when combined with a pacifier.25 The infants treated with sucrose showed less signs of distress and cried less than infants who did not receive sucrose.26 A 24% sucrose solution can be compounded and unit-dose packaged into 2-mL doses in oral syringes, and stocked in patient-care areas such as the newborn nursery or newborn intensive care unit. The sucrose is administered on the infant's tongue over 1 minute just prior to the procedure. The duration of action is about 5 minutes and there are no side effects.

Environment can play a significant role in how a child reacts to pain or a medical procedure. The chaotic atmosphere of an ED can be scary to a child. Placing the child in a calm environment minimizes distress.26 A private room with colorful walls and pictures, a collection of toys or games, music, or videos can minimize fear. Even blowing bubbles or blowing on a pinwheel helps to reduce stress.

One of the best examples of nonpharmacologic techniques that I have observed involved my youngest son, Steven. He was running around at the babysitter's house and fell into her piano, splitting open his upper eyelid. The babysitter did a great job calming him down and butterflying the wound, but I still had to take him to the ED for stitches. The nurse put us in a quiet area of the ED with curtains completely surrounding his gurney. Even though the wound was very nasty looking, the physician and nurse showed no negative emotion and talked playfully to Steven throughout the entire suturing procedure. Before the suturing began, the nurse brought a large white sheet into the room, told Steven that it was a magic cape just like Batman or Superman wears, and he was going to wear this magic cape. He was snugly wrapped in the sheet, laughing because it was really a game for him. The physician draped Steven's eyelid to isolate the wound and blind Steven from the sight of the needles and syringe. The physician did warn Steven that he may feel a pinch or two, but Steven still remained calm and talkative. The lidocaine infiltration was administered, six sutures were done, and not a single tear was shed by Steven or Mom. When the procedure was all done and the "magic" cape was removed, Steven proudly asked in his high, squeaky 3-year-old voice, "I was a very...

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LIDOCaine, Epinephrine, TetraCaaine (LET) Sterile Gel

For 75 x 5-mL single-use syringes

| Lidocaine hydrochloride powder | 16 g |
| Epinephrine hydrochloride 1:1000 injectable | 200 mL |
| Tetracaine hydrochloride powder | 2 g |
| 3% Carboxymethylcellulose in isotonic saline sterile gel | 180 mL |

Note: This formulation should be prepared according to strict aseptic compounding technique in a laminar airflow hood in a cleanroom or via isolation barrier technology by a compounding pharmacist who is validated in aseptic compounding. This is a low-risk preparation.

METHOD OF PREPARATION

1. Sterilize 75 amber oral/topical syringes with caps. Note: The syringes and caps may be gas-sterilized or irradiated.
2. Weigh and/or measure each ingredient accurately.
3. Add the powders to the epinephrine solution in a beaker and mix well to dissolve.
4. Draw up the solution with a sterile syringe, attach an appropriate 0.22-micron filter, and filter the solution into a sterile top-fill bag.
5. Add the pre-made carboxymethylcellulose gel to the top-fill bag, cap, and gently shake the bag to evenly mix the solution and gel.
6. Attach a sterile fluid transfer set on the top-fill bag and to the peristaltic pump.
7. Attach a sterile Luer-lock-to-oral connector to the end of the transfer set.
8. Pump 5 mL of gel into a sterile, amber oral/topical syringe, cap, and label the syringe.

STABILITY AND STORAGE

LET gel is stable for 154 days refrigerated and must be protected from light. Note: Stability information obtained from Baxter Corporation's Product Catalog.

Conclusion

Medical procedures do not have to be painful. There are several pharmacologic options available, both commercial and compounded, for providing local anesthesia and minimizing the fear and stress associated with these procedures. No patient should suffer because the clinician lacks the knowledge or comfort level necessary to provide adequate analgesia during painful medical procedures. Compounding pharmacists can prepare local and topical anesthetics for clinics, EDs,
REFERENCES


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