Use of Topical Anesthetics To Support Intubation

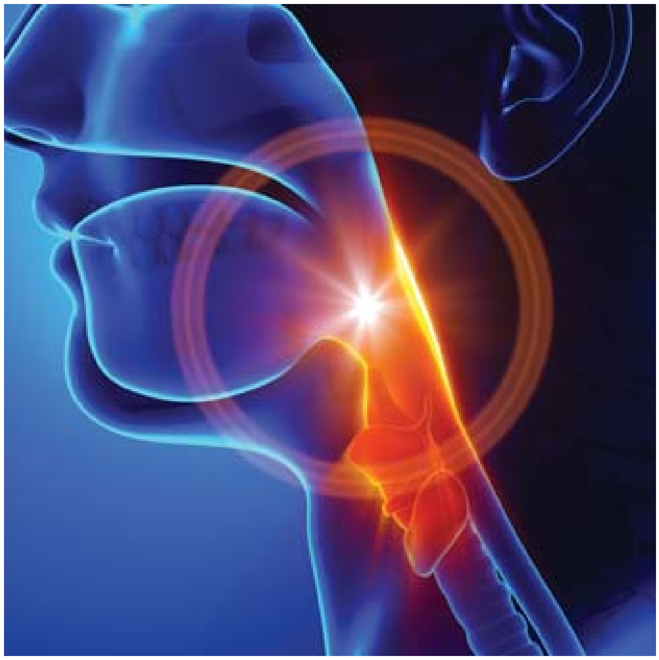
Faculty Reviewers

Carlos Artime, MD
Assistant Professor
Department of Anesthesiology
The University of Texas Health Science Center at Houston
Houston, Texas

Kenneth Candido, MD
Chairman
Department of Anesthesiology
Advocate Illinois Masonic Medical Center
Chicago, Illinois

Julie Golembiewski, PharmD
Clinical Associate Professor
Clinical Pharmacist
University of Illinois College of Medicine at Chicago
Chicago, Illinois

Tricia Meyer, PharmD
Associate Professor of Anesthesiology
Texas A&M University College of Medicine
Bryan, Texas



The faculty reviewers reported no relevant financial disclosures. The medical writer, Lynne Peeples, also reported no relevant financial disclosures.

Topical anesthetic products can play a pivotal role in the comfort and safety of patients in the operating room. When used in conjunction with awake intubation, for example, and delivered with skill and care, these agents can lessen or even eliminate the need for sedation, thereby greatly improving patient cooperation during surgical procedures.

By reversibly anesthetizing the nerve endings near the site of administration, topical anesthetics produce a transient and localized loss of sensation and, therefore, can decrease pain and discomfort during procedures in the operating room (OR). Topical anesthetics are generally only effective on intact mucosal surfaces, such as those inside the mouth, nose, eyes, throat, genitals, and other inner body surfaces.

Topicalization of the Airway Prior to a Procedure

One of the most common uses of topical anesthetics in the OR is to prepare a patient for endoscopy, intubation, bronchoscopy, or a similar invasive airway procedure. Applying a topical anesthetic inside the throat before inserting a tube or scope can suppress the gag reflex, especially in an awake patient. For patients with a difficult airway, such as those with large glottic tumors or with an unstable cervical spine, securing the airway before induction of general anesthesia can minimize the risk for major airway-related complications, such as hypoxic brain damage and death.[1]

The most common topical anesthetics for airway indications include atomized or nebulized spray preparations of lidocaine and benzocaine, alone or in combination with tetracaine. Preparations can differ in administration method, focus of application (oral or nasal route), speed of onset, length of action, and safety. Given the growing awareness of the increased risk for methemoglobinemia associated with use of some benzocaine formulations, clinicians may prefer lidocaine to obtain airway anesthesia.[2]

Formulations

The first topical anesthetic, cocaine, was prepared for clinical use in the latter half of the 19th century.[3] Today, clinicians have a choice of several relatively safe and effective anesthetic products, available as regular or viscous solutions, gels, ointments, and in spray cans. Lidocaine and benzocaine, alone or in various combinations with cocaine, prilocaine, tetracaine, and epinephrine are the formulations most commonly found in the OR (Table 1).

Lidocaine

An amide anesthetic, lidocaine has a rapid onset of clinical activity of about 2 to 5 minutes and its effects typically last from 15 to 60 minutes or more.[4] The drug is available in various concentrations, including 1%, 1.5%, 2%, and 4%, and can come with or without epinephrine. Combination formulations may be appropriate when vasoconstriction is desired, such as during nasal topicalization. Lidocaine's liquid form can be nebulized or atomized, which can be ideal for spraying an anesthetic directly into the airway. Ointments and gels are also available. Up to 8 mg/kg of body weight is generally considered safe for application of lidocaine to the airway.

Benzocaine

Benzocaine is an ester local anesthetic with a very fast onset of action within 1 minute.[5] Compared with lidocaine, however, its duration of action is also shorter—between 5 and 15 minutes.[6] The drug is available in various preparations and is administered via different devices.

HurriCaine (Beutlich) is comprised of benzocaine (20%).[7] Again, onset is fast (<1 minute) and duration is generally around 15 minutes. HurriCaine One contains the same formula as HurriCaine, but comes unit-dosed as opposed to a 30-mL bottle.

Exposure to benzocaine may result in toxic effects, such as methemoglobinemia (see section on methemoglobinemia, page 53, for more information on this adverse reaction).

Benzocaine/Butamben/Tetracaine

Cetacaine (Cetalyte) is a prescription commercial spray that includes a mixture of benzocaine (14%), butamben (2%), and tetracaine (2%).[8] The latter is another potent anesthetic of the ester class. In combination, the anesthetics provide relatively fast action (<1 minute) and moderate duration (30-60 minutes). The spray formulation should be applied for one second or less, not to exceed 2 seconds. It is available in spray, liquid, or gel forms.

Drug Administration

In addition to direct application of gels, creams, and ointments, topical anesthetics are also commonly administered as a liquid via various delivery devices.

Atomization devices are designed to deliver topical anesthesia into nasal, oral, pharyngeal, laryngeal, and

Table 1. Common Topical Formulations

Chemical Name	Composition	Onset and Duration of Action	Clinical Considerations
Benzocaine (various; HurriCaine; HurriCaine One	Ester class anesthetic; various strengths; HurriCaine formulations at 20%	Onset: <1 min Duration: 5-15 min	• Commonly used for topicalizing the airway prior to a procedure • Reports of methemoglobinemia; HurriCaine One (unit-dosed) may decrease risk associated with longer sprays
Benzocaine/ Butamben/ Tetracaine (Cetacaine)	Prescription spray: benzocaine (14%), butamben (2%), tetracaine (2%)	Onset: <1 min Duration: 15-30 min	• Limit to <2 sec of spray • Reports of methemoglobinemia
Lidocaine	Amide class anesthetic Most common solutions: 1%, 1.5%, 2%, and 4%	Onset: 2-5 min Duration: 15-60 min	• Commonly used for topicalizing the airway prior to a procedure and anesthetizing skin prior to a cutaneous puncture • Formulations with added epinephrine can help achieve vasoconstriction • Adverse reactions more common in patients with heart disease • Reports of methemoglobinemia

tracheal tissues (Table 2). The devices deliver atomized droplets of the liquid anesthetic. Depending on the device, it can be difficult to gauge just how much of the anesthetic is being delivered into the patient. Mucosal atomization devices, such as the LMA MADgic (Teleflex), produce a relatively tight stream of atomized droplets and include a syringe with volume markers, allowing for more precise dosing. Also of concern with atomization devices is the potential loss of some anesthetic into the atmosphere during administration.

Nebulizers tend to produce smaller droplets than atomization devices. Used with standard settings, these droplets are so fine that they often settle into the deepest part of the lungs rather than the upper airway. To create larger droplets that reach the upper airway, a nebulizer's oxygen flow rate can be lowered.

A strategy used by clinicians is to begin anesthetizing a patient with a small amount of nebulized anesthetic, such as lidocaine, at low flow rates, to provide background numbing. Then they may transition to an atomization device to target sensitive areas, such as around the vocal cords and lower pharynx.

Some clinicians may also choose to apply a cotton pledget soaked in local anesthetic to targeted mucosal surfaces to achieve a selective blockade of underlying nerves. More direct nerve blocks in the airway can be achieved using needle-based techniques. Some clinicians advocate using such blocks in conjunction with topical anesthetics; others prefer using topicals exclusively. If needle blocks are used, it is important to note that the technique may be contraindicated in certain patients, such as those with coagulopathies and/or who are being treated with anticoagulants.[9] Additionally, the blocks can cause complications, including bleeding, nerve injury, and seizures from intravascular injection.[4] For more details on the use of needle-based airway blocks, see the review by the New York School of Regional Anesthesia.[10]

Additional airway strategies can help maximize the effectiveness of topical anesthetics. For nasal intubation, adding vasoconstrictors such as epinephrine at a concentration of 1:200,000, or phenylephrine at a concentration of 0.05%, to the local anesthetic can prolong the topical anesthetic effect and help reduce mucosal bleeding. Also, the administration of glycopyrrolate can help reduce the production of saliva, which acts as a barrier between the anesthetic agent and the mucosa.

Safety Considerations

Allergic Reactions

It is rare for a patient to be allergic to a topical anesthetic, especially those of the amide class such as lidocaine. Actual hypersensitivity reactions account for less than 1% of all reactions to local anesthetics.[11,12] The amount of drug administered and the route of administration can influence the side effects of topical anesthetic agents. Care should be taken with topical anesthetics to ensure that the predetermined amount of the drug is administered to produce the intended effect while also minimizing the risk for toxicity.

An allergic reaction to certain topical anesthetics, more often those of the ester than the amide class, may manifest on the skin as mild redness and burning to discoloration and swelling. More serious side effects, such as tissue necrosis and sloughing of the skin, have also been reported.[13]

Central Nervous System Effects

High plasma concentrations of anesthetics can stimulate the central nervous system (CNS), potentially causing seizures. This can be followed by CNS depression, including respiratory arrest. Solutions that contain epinephrine may add to the CNS stimulatory effect, which may be confused with a bona fide allergic type of reaction.[14-16]

Life-threatening adverse effects have been known to occur following topical anesthetic application over large areas of the body, especially when plastic occlusives are applied to enhance absorption.[17] The FDA issued an advisory on the potentially life-threatening side effects of topical anesthetics after 2 women experienced seizures, coma, and death after applying topical anesthetics to their legs with an occlusive dressing before laser hair removal.[17] Caution is also warranted when applying local anesthetics to mucosal areas.

Cardiovascular Effects

High plasma levels of anesthetics may depress heart function and result in bradycardia, arrhythmias, hypotension, cardiovascular collapse, and cardiac arrest.[18] Anesthetics that contain epinephrine can trigger hypertension, tachycardia, and angina.

Methemoglobinemia

Methemoglobinemia occurs when iron in hemoglobin is transformed from ferrous to ferric form, or methemoglobin. Unlike hemoglobin, methemoglobin is unable to transport oxygen to body tissues. The resulting oxygen deprivation can affect the CNS and cardiovascular system, manifesting as lightheadedness, confusion, hypoxia, and cyanosis.[19] Acquired methemoglobinemia can be life-threatening, but early recognition and treatment will greatly improve outcomes in this reversible condition. Methemoglobinemia can be identified via symptoms or the use of a pulse CO oximeter, such as the Rad-57 (Masimo).[20] With significant methemoglobinemia, the oxygen saturation will trend toward 85% on standard pulse oximetry. An IV dose of 1 to 2 mg/kg of methylene blue is usually enough to reverse methemoglobinemia.[21] Transfusion or dialysis is preferred for patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency because methylene blue can trigger hemolytic anemia.

Prevention of methemoglobinemia is preferable, of course. Using multiple sprays of an agent or spraying the area for a longer duration than recommended is often the culprit in cases of methemoglobinemia. Unclear package instructions, or application by clinicians unfamiliar with the significant absorption of topical anesthetics, may lead to overdoses. For some patients, however, even tiny amounts—well within recommended dosing—can result in clinically significant methemoglobinemia. Numerous case reports have been reported involving as little as 1 second of spraying of Cetacaine or delivery of 15 to 25 mg/kg of benzocaine.[22,23]

Up to 1 in every 370 patients will be particularly susceptible to developing methemoglobinemia, likely due to genetic variation.[24] Infants under age 6 months, older patients, and individuals with respiratory or cardiac disease may also be sensitive to low methemoglobin levels.[23] Clinical situations such as anemia or hypoalbuminemia can raise the risk.[25] A Johns Hopkins study found 138 patients with raised methemoglobin levels during a 28-month period.[26] If the area being sprayed is inflamed or the skin is broken, a larger volume of the drug may be absorbed than was intended. Concomitant use of other drugs, such as isosorbide dinitrate, can also increase the likelihood of methemoglobinemia.[25]

The anesthetic most commonly associated with the condition is benzocaine. Reports received by the FDA

Table 2. Atomization Devices

Name (Manufacturer)	Description	Size
DeVilbiss Model 15 Medical Atomizer (DeVilbiss Healthcare)	Metal atomizer; includes glass receptacle (for liquid), pair of metal outlet tubes extending from metal atomizing nozzle, and adjustable tip for directing spray to inaccessible areas of the throat. Can be used with or without RhinoGuard tip cover.	Length: 10.5 in.
Enk Fiberoptic Atomizer Set (Cook Medical)	Device for atomizing small doses of local anesthetics. Atomizer set consists of a pressure-resistant oxygen tube and a connecting tube attached by a 3-way side-arm fitting with a small flow control opening. The set also contains an introducer catheter and 2 syringes (1 mL).	
EZ-Spray (Alcove Medical)	Disposable atomizer device that comprises a plastic receptacle, atomizer nozzle, and gas inlet tube. Tubing is connected from an air or oxygen flowmeter nipple to the gas inlet tube on the device.	
LMA MADdy Pediatric Mucosal Atomization Device (Teleflex)	Delivers intranasal/intraoral medications in a fine mist that enhances absorption and improves bioavailability for fast and effective drug delivery.	Typical particle size: 30 microns. System dead space: 0.12 mL (with syringe), 0.07 mL (device only). Tip diameter: 0.19 in (4.8 mm). Applicator length: 4.5 in (11.4 cm).
LMA MADgic Airway Intubating Airway with Mucosal Atomization and Oxygen Delivery (Teleflex)	For difficult and awake airways requiring a fiber-optic scope, the device combines atomized topical anesthetic and oxygen delivery in an innovative and elegantly designed fiber-optic–compatible oral airway.	Typical particle size 30-100 microns. System dead space 0.15 mL. Oxygen flow rate 2-3 L/min at 50 psi. Size 9 cm airway (6.5-8.0 ET).
LMA MADgicWand Mucosal Atomization Device (Teleflex)	Combines atomized topical anesthesia and oxygen delivery in a fiber-optic oral airway. Packaged in box of 20.	Typical particle size: 30-100 microns. System dead space: 0.25 mL.
LMA MADgic Laryngo-Tracheal Atomizer (Teleflex)	Mucosal atomization device that incorporates a small flexible, malleable tube with an internal stiffening stylet that connects to 3-mL syringe.	Typical particle size: 30-100 microns. System dead space: 0.25 and 0.13 mL. Tip diameter: 0.18 in (4.6 mm). Applicator length: 8.5 in (21.6 cm) and 4.5 in (11.4 cm).
LMA MAD Nasal-Intranasal Mucosal Atomization Device (Teleflex)	Disposable, compact atomizer for delivery of medications to the nose and throat in a fine, gentle mist.	Typical particle size: 30-100 microns. System dead space: 0.13 and 0.07 mL. Tip diameter: 0.17 in (4.3 mm). Applicator length: 1.65 in (4.2 cm).

between November 1997 and March 2002 described 132 cases of benzocaine-induced methemoglobinemia. Most of the cases (93.2%) involved benzocaine spray. Furthermore, of the 69 cases that specified a dose, 37 (53.6%) indicated that only a single spray was applied.[27]

The total number of benzocaine-induced cases of methemoglobinemia in the literature is in the hundreds, and this likely represents an underestimation of the actual number of cases.[28] Because of the greater risk for methemoglobinemia, Veterans Administration (VA) hospitals have banned benzocaine in favor of lidocaine.[29] A VA report describing 35 reported cases of methemoglobinemia, however, did link more of those cases (6 or 17%) to the use of lidocaine than to Cetacaine (4 or 11%).[28] The majority of the cases were attributed to generic benzocaine (24 or 69%). It has been theorized that the lower rate of methemoglobinemia seen with Cetacaine may be due to the prescription product being designed to deliver a more precise quantity of benzocaine and at a lower concentration than is the case with generic formulations. However, published evidence for that is lacking.

Clinical Applications	Special Features
Intended for the application of topical anesthetics to the nose, oropharynx, and upper airway of patients, at the direction/discretion of a clinician.	Includes glass receptacle for dispensing the liquid; adjustable swivel top and vented nasal guard attached to a hand bulb. Can be used with all types of oil or water solutions that are compatible with rhodium metal plating. The all-metal top can be autoclaved. Reusable.
To apply topical anesthetics to laryngotracheal area through the working channel of a bronchoscope using oxygen flow. Designed and intended for use by those trained and experienced in techniques of flexible fiber-optic intubation.	An accessory to a bronchoscope. Delivery form: fine spray mist using oxygen flow through the working channel bronchoscope. Sterile. Single use.
Application of topical anesthetic to the nose, oropharynx, and upper airway of patients, at the direction/discretion of a clinician.	Trigger-valve system provides controlled release of compressed gas to atomizing nozzle, creating liquid spray. Gas flow adjusted to desired setting. Use with either oil- or water-based solutions. Nonsterile. Single use.
Application of topical anesthetics to oropharynx and upper airway region. Fits through vocal cords, down LMA, or into nasal cavity.	Child-friendly and no sharps (bright colors in a toylike presentation make procedure less scary for young patients). Flexible (internal stylet provides support, malleability, and memory). Disposable (single-patient use eliminates risk for cross-contamination). Practitioner-controlled (patient needs targeted specially by medication, concentration, position, and location).
For use with fiber-optic bronchoscopy.	Intubating airway with mucosal atomization and oxygen delivery.
Allows retraction of soft tissue while applying topical anesthesia in a fine, gentle mist. Used to apply topical anesthetic to the airway before awake intubation.	Device blade positioned along floor of the mouth can be directed immediately in front of laryngeal inlet to generate a fine mist by a piston syringe. Nonsterile. Single use.
Application of topical anesthetics to oropharynx and upper airway region. Fits through vocal cords, down LMA, or into nasal cavity.	Malleable applicator retains memory to adapt to individual patient's anatomy. Delivery of a fine spray mist generated by a piston syringe. Luer connection adapts to any luer lock syringe. Nonsterile. Single use.
Intranasal medication delivery offers rapid, effective method to deliver selected medications to patient without need for a painful shot and without delays in onset seen with oral medications.	Rapidly effective (atomized nasal medications absorb directly into bloodstream, avoiding first-pass metabolism; atomized nasal medications absorb directly into the brain and cerebrospinal fluid via olfactory mucosa to nose–brain pathway, achieves medication levels comparable to injections). Controlled administration (exact dosing, exact volume, titratable to effect [repeat if needed]; atomizes in any position; atomized particles are optimal size for deposition across broad area of mucosa).

Clinicians can follow several strategies to reduce the risk for methemoglobinemia, including accurately documenting the amount of drug administered (Table 3).

The Pharmacist's Role

Pharmacists can play a significant role in ensuring topical anesthetic products are chosen, dated, stored, and administered appropriately. A pharmacist might, for example, look at the safety and efficacy of various products, alongside a cost table, to make the most cost-effective choice for his or her institution. The pharmacist can also label and store preparations for topical use in a way so that they are not unintentionally administered incorrectly. By posting maximum doses and educating staff on the signs and symptoms of methemoglobinemia and systemic absorption, as well as on how to prevent and treat the condition, a pharmacist can help to prevent further cases at his or her institution.

References

1. Hagberg C. Current concepts in the management of the difficult airway. *Anesthesiology News*. 2015;41(5). anesthesiologynews.com/ViewArticle.aspx?d=Educational+Reviews&d_id=161&i=May+2015&i_id=1183&a_id=32361. Accessed July 21, 2015.
2. Vailurupalli S, Manchanda S. Risk of acquired methemoglobinemia with different topical anesthetics during endocscopic procedures. *Local Reg Anesth.* 2011;4:25-28.
3. Doyle D. Topical and Regional Anesthesia For Tracheal Intubation. *Anesthesiology News Guide To Airway Management.* 2014. http://anesthesiologynews.com/download/Topicals_ANGAM14_WM.pdf. Accessed July 21, 2015.
4. www.drugs.com/mtm/lidocaine-topical.html. Accessed July 21, 2015.
5. Ruetsch YA, Boni T, et al. From cocaine to ropivacaine: the history of local anesthetic drugs. *Curr Top Med Chem*. 2001;1(3):175-182.
6. Hagberg C. Benumof and Hagberg's Airway Management. 3rd ed. Philadelphia, PA: Saunders Elsevier; 2013.
7. beutlich.com/product-sheets. Accessed July 21, 2015.
8. www.cetacaine.com/dental/about/prescribing-information. Accessed July 21, 2015.
9. Jeng CL, Torrillo TM, Rosenblatt MA. Complications of peripheral nerve blocks. *Br J Anaesth.* 2010;105 Suppl 1:i97-i107.
10. Regional & topical anesthesia for endotracheal intubation. New York School of Regional Anesthesia. www.nysora.com/techniques/nerve-stimulator-and-surface-based-ra-techniques/head-and-neck-blocka/3022-regional-topical-anesthesia-for-endotracheal-intubation.html. August 2013. Accessed July 20, 2015. (*Note that dexmedetomidine dose in the article is incorrect. It should be loading dose: 1 mcg/kg over 10 min, infusion rate: 0.2-0.7 mcg/kg per hour.*)
11. McEvoy GK, Miller J. Antipruritics and local anesthetics. AHFS Drug Information. Bethesda, MD: American Society of Health-System Pharmacists, Inc; 2007.
12. Wolters Kluwer Health, Inc. Local anesthetics, topical. *Drug Facts & Comparisons*. eFacts [online]. 2007.
13. Zempsky WT, Karasic RB. EMLA versus TAC for topical anesthesia of extremity wounds in children. *Ann Emerg Med*. 1997;30(2):163-166.
14. Daya MR, Burton BT, et al. Recurrent seizures following mucosal application of TAC. *Ann Emerg Med*. 1988;17(6):646-648.
15. Mercado P, Weinberg GL. Local anesthetic systemic toxicity: prevention and treatment. *Anesthesiol Clin*. 2011;29(2):233-243.
16. Becker DE, Reed KL. Essentials of local anesthetic pharmacology. *Anesth Prog*. 2006;53(3):98-108.
17. US Food and Drug Administration. Public health advisory: life-threatening side effects with the use of skin products containing numbing ingredients for cosmetic procedures. www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm054718.htm. February 6, 2007. Accessed July 5, 2015.
18. Lin F, Chang W, et al. Cardiovascular complications resulting from topical lidocaine application. *Int J Gerontol*. 2008;2(4):229-232.
19. Wilburn-Goo D, Lloyd L. When patients become cyanotic: acquired methemoglobinemia. *JADA.* 1999;130:826- 831.
20. Barker SJ, Curry J, Redford D, et al. Measurement of carboxyhemoglobin and methemoglobin by pulse oximetry: a human volunteer study. *Anesthesiology.* 2006;105(5):892.
21. Sikka P, Bindra VK, Kapoor S, et al. Blue cures blue but be cautious. *J Pharm Bioallied Sci.* 2011;3(4):543-545.
22. Ellids FD, Seiler JG, Palmore MM. Methemoglobinemia: a complication after fiberoptic orotracheal intubation with benzocaine spray. A case report. *J Bone Joint Surg Am.* 1995;77-A(6):937-939.
23. Khorasani A, Candido KD, Ghaleb AH, et al. Canister tip orientation and residual volume have significant impact on the dose of benzocaine delivered by hurricaine spray. *Anesth Analg.* 2001;92:379-383.
24. Novaro GM, Aronow HD, et al. Benzocaine-induced methemoglobinemia: experience from a high-volume transesophageal echocardiography laboratory. *J Am Soc Echocardiogr.* 2003;16:170-175.
25. Vallurupalli S. Methemoglobinemia due to topical pharyngeal anesthesia during endoscopic procedures. *Local Reg Anesth.* 2010;3:137-142.
26. Ash-Bernal R, Wise R, Wright SM. Acquired methemoglobinemia: a retrospective series of 138 cases at 2 teaching hospitals. *Medicine (Baltimore)*. 2004;83:265-273.
27. Moore TJ, Walsh CS, Cohen MR. Reported adverse event cases of methemoglobinemia associated with benzocaine products. *Arch Intern Med*. 2004;164(11):1192-1196.
28. US Department of Veterans Affairs. A guidance on the use of topical anesthetics for naso/oropharyngeal and laryngotracheal procedures. www.pbm.va.gov/PBM/clinicalguidance/criteriaforuse/benzocaine.pdf. February 2006. Accessed July 5, 2015.
29. Rodriguez LF, Smolik LM, Zbehlik AJ. Benzocaine-induced methemoglobinemia: report of a severe reaction and review of the literature. *Ann Pharmacother*. 1994;28(5):643-649.

Table 3. Minimizing the Risk for Methemoglobinemia

Apply labels to topical anesthetic spray bottles to warn staff of dangers of excessive use in patients.
Ask questions when taking a patient's medical history to identify risk factors.
Document the amount of drug being administered, including measuring and recording the number and duration of sprays applied. (A reference chart listing maximum doses for topical anesthetics can be helpful.)
Keep supplemental oxygen and methylene blue on hand wherever topical anesthetics are used in patients.
Opt for delivery devices that provide more precision in drug administration.
Stock only 1 topical anesthetic product to reduce confusion with regard to dosing. Lidocaine may be a safer choice than benzocaine.