Topical Anesthetic-Induced Methemoglobinemia

Healthcare professionals know that intravenous or inhaled anesthetics are not innocuous substances. Yet, the widespread availability of anesthetics like benzocaine, dyclonine, and lidocaine in many topical over-the-counter (OTC) products, such as Cepacol® Anesthetic Troches and Sucrets® Maximum Strength Lozenges may lead to the perception of their safety. Many topical anesthetic sprays such as CETACAINE (benzocaine 14%, tetracaine 2%) and HURRICANE (benzocaine 20%) have been implicated in cases of methemoglobinemia, a serious and sometimes fatal adverse drug reaction.

Methemoglobinemia occurs when iron in hemoglobin is changed from its ferrous to its ferric form. Unlike hemoglobin, methemoglobin cannot accept oxygen to carry to tissues. It can be hereditary, but methemoglobinemia is typically acquired from drugs and chemicals, such as nitrites and aniline derivatives, which includes virtually all local anesthetics. The condition can be life-threatening, potentially causing cyanosis, confusion, hemodynamic instability, and coma if not recognized and treated appropriately. Methemoglobin concentrations greater than 10-15% of total hemoglobin will cause cyanosis, and levels over 70% have been fatal. Identifying this condition while administering topical anesthetics such as benzocaine usually requires pulse oximetry, though it can be implied by symptoms. Treatment involves an immediate intravenous (IV) dose of 1 to 2 mg/kg of methylene blue.

PA-PSRS has received multiple reports in which patients receiving Hurricane or Cetacaine topical spray have required treatment with methylene blue. Following are a few examples:

During intubation, benzocaine spray was administered to a patient, who then developed decreased oxygen saturation to 89%. The patient was diagnosed with methemoglobinemia and subsequently treated with methylene blue.

Hurricane Topical Spray was used at the initiation of a procedure, and the patient experienced decreased oxygen saturation during recovery in the Post Anesthesia Care Unit. Because methemoglobinemia was suspected, methylene blue was administered, which increased the oxygen saturation.

Topical oral cetacaine spray was administered to a patient who was desaturating while on a 100% aerosol tracheotomy mask with oxygen saturations in the low 80’s. The patient continued to be cyanotic despite multiple interventions. Fortunately methemoglobinemia was diagnosed, and the patient was treated with methylene blue.

Doses of topical anesthetics administered during endoscopic procedures may exceed manufacturers’ recommendations for several reasons. First, unclear package instructions for using the products may lead to overdoses. The directions for use of topical sprays are prone to misinterpretation and could result in patient harm. A portion of one label states, “Spray in excess of two seconds is contraindicated,” but the directions state, “To activate spray, press cannula in any direction with forefinger for approximately one second. Maximum anesthesia is produced in one minute” (meaning one minute after a quick spray). This...
Topical Anesthetic–Induced Methemoglobinemia (Continued)

could be misinterpreted to mean that a continuous spray of up to one minute is permitted, even desirable, for maximum anesthesia.

Clinicians may be unfamiliar with the significant absorption of topical anesthetics, so they may not realize how much medication they are giving patients when using the sprays. Patients also could self-administer topical anesthetics in doses that exceed manufacturers’ recommendations. Since some products are available without a prescription (e.g., Hurricane), a patient could apply too much spray or gargle too often with a liquid formulation (or swallow the solution), since the directions for use may be vague (e.g., “apply a small amount”). Methemoglobinemia has also occurred when an OTC vaginal cream was used to treat an infant’s diaper rash.8

Because methemoglobinemia is easily treated, it is important to recognize its symptoms when topical anesthetics are used. Heightened awareness of proper dosing and the risk of methemoglobinemia is particularly important for clinicians involved in endoscopy, intubation, bronchoscopy, or similar invasive procedures using topical anesthetic-containing sprays. These drugs are not intended to be used in high doses, especially in patients who may be predisposed to methemoglobinemia.

Predisposing factors for methemoglobinemia include:

- Age (infants under 6 months of age and older patients with cardiac problems may be sensitive to even low methemoglobin levels).
- The status of the area being sprayed (inflamed areas and broken skin absorb more of the drug).
- Concomitant use of other drugs which also have been implicated in causing methemoglobinemia.
- The genetic make-up of the patient (due to altered hemoglobin, G6PD deficiency, or methemoglobin reductase enzyme deficiency).9

To help avoid adverse outcomes associated with this problem, consider the following strategies:

- Asking questions while taking the medical history to identify these risk factors in patients who may receive topical anesthetics.
- To document the amount of drug being administered, measuring and recording the number and duration of sprays applied. A chart that lists maximum doses for topical anesthetics also may be helpful as a reference for staff that perform endoscopic procedures.
- Stocking just one topical anesthetic spray also could enhance staff familiarity with the product and its’ dosing.
- If cyanosis or hypoxia develops after the application of topical anesthetics, consider a diagnosis of methemoglobinemia.
- Having supplemental oxygen and methylene blue readily available to treat methemoglobinemia wherever topical anesthetics are used in the facility.
- It also may be helpful to apply auxiliary labels to topical anesthetic spray bottles to alert staff to avoid excessive use.

A metered-dose product is currently available (20% benzocaine). However, even a metered-dose product will not prevent an overdose if multiple sprays are used.

Notes
The Patient Safety Authority is an independent state agency created by Act 13 of 2002, the Medical Care Availability and Reduction of Error (“Mcare”) Act. Consistent with Act 13, ECRI, as contractor for the PA-PSRS program, is issuing this newsletter to advise medical facilities of immediate changes that can be instituted to reduce serious events and incidents. For more information about the PA-PSRS program or the Patient Safety Authority, see the Authority’s website at www.psa.state.pa.us.

ECRI is an independent, nonprofit health services research agency dedicated to improving the safety, efficacy and cost-effectiveness of healthcare. ECRI’s focus is healthcare technology, healthcare risk and quality management and healthcare environmental management. ECRI provides information services and technical assistance to more than 5,000 hospitals, healthcare organizations, ministries of health, government and planning agencies, and other organizations worldwide.

The Institute for Safe Medication Practices (ISMP) is an independent, nonprofit organization dedicated solely to medication error prevention and safe medication use. ISMP provides recommendations for the safe use of medications to the healthcare community including healthcare professionals, government agencies, accrediting organizations, and consumers. ISMP’s efforts are built on a non-punitive approach and systems-based solutions.