Benzocaine Topical Sprays and Methemoglobinemia

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**PROBLEM:** Topical anesthetic sprays such as benzocaine 14%, tetracaine 2% (Cetacaine®, Cetylite Industries) and benzocaine 20% (Hurricane®) have been implicated in cases of methemoglobinemia. Because methemoglobin is a form of hemoglobin that is unable to carry oxygen, the condition can be life-threatening, causing cyanosis, confusion, hemodynamic instability, and coma if it is not recognized and treated appropriately.

As of 2002, the Medwatch database of the Food and Drug Administration (FDA) contained approximately 100 reports of methemoglobinemia related to the use of benzocaine, the most common topical anesthetic associated with this reaction. However, this is probably only a small fraction of actual cases experienced in the U.S. It is well known that spontaneous reports sent to Medwatch severely underestimate the actual number of occurrences of specific drug-related problems. For example, methemoglobinemia occurs during one of every 7,000 bronchoscopies.

One article analyzing adverse drug event (ADE) reports received by the FDA between November 1997 and March 2002 revealed 132 cases of benzocaine-induced methemoglobinemia. Given that millions of doses of topical anesthetics are administered during endoscopic procedures and endotracheal intubation, methemoglobinemia is probably not a rare occurrence.

In reviewing reported cases of methemoglobinemia, clinicians often used multiple sprays of benzocaine and sprays of longer duration than recommended. Doses administered during endoscopic procedures can exceed the manufacturer’s recommendations for several reasons:

- First, unclear package instructions for using the products may lead to overdoses. In 2002, the Institute for Safe Medication Practices mentioned that the directions for use of Cetacaine® topical spray were prone to misinterpretation and could result in patient harm. One portion of the label states: “Spray in excess of two seconds is contraindicated.” However, the directions state: “To activate spray, press Jetco-Spray Cannula in any direction with forefinger for approximately one second. Maximum anesthesia is produced in one minute.” This phrasing could be misinterpreted to mean that a continuous spray of up to one minute is permitted, even desirable, for maximum anesthesia. Cetylite has now updated the label: “Spray should be applied for approximately one second or less for normal anesthesia . . . Spray in excess of two seconds is contraindicated.”

- Second, clinicians might not be familiar with the significant absorption of topical anesthetics and thus might not realize just how much medication they are giving patients when these sprays are being used.

- Third, patients might self-administer topical anesthetics in doses that exceed the manufacturer’s recommendations. Because some products, such as Hurricane®, are available without a prescription, patients might apply too much spray or they might gargle too often with a liquid formulation or swallow the solution, especially because the directions for use are vague (e.g., “apply a small amount”).

**SAFE PRACTICE RECOMMENDATION:** Clinicians and patients should be alerted to the proper dosing of topical anesthetics and the possibility of methemoglobinemia when these products are used. These drugs should not be used in high doses, especially with patients who might be predisposed to methemoglobinemia. Predisposing factors include:

- age. Infants younger than six 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 absorb more drug.
- the concomitant use of other drugs that also have been implicated in causing methemoglobinemia.
- the genetic makeup of the patient (because of altered hemoglobin, glucose-6-phosphate dehydrogenase [G6PD] deficiency, or methemoglobin reduc-tase enzyme deficiency).

In summary, clinicians should obtain a medical history for patients who are to receive topical anesthetics in order to determine the presence of any risk factors.

**REFERENCES**


The reports described in this column were received through the USP–ISMP Medication Errors Reporting Program (MERP). Errors, close calls, or hazardous conditions may be reported on the ISMP (www.ismp.org) or the USP (www.usp.org) Web site or communicated directly to ISMP by calling 1-800-FAIL SAFE or via e-mail at ismpinfo@ismp.org.