Benzocaine Spray and Methemoglobinemia

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Objectives

- At the end of this learning module, the learner will be able to:
  - Define Methemoglobinemia.
  - Verbalize agents that may trigger the methemoglobinemia condition.
  - Identify the clinical signs/symptoms of methemoglobinemia.
  - Explain appropriate actions to counteract the methemoglobinemia condition.
Before placing a nasogastric tube in a 74-year-old man, a physician administered three sprays of HURRICANE (20% benzocaine), 1-2 seconds each, to numb the patient’s throat. An hour later, the patient became hypoxic and did not improve despite receiving oxygen. A blood gas was drawn, which had a chocolate appearance, prompting an order for a methemoglobin level. The result was 46% (normal is less than 1%). Methylene blue was infused and 2 hours later, the patient’s methemoglobin level was normal at 0.9%.” 2009, ISMP, 7(2)
What is Methemoglobinemia?

“A condition evidenced by abnormal levels of oxidized hemoglobin. The oxidized hemoglobin binds so firmly with oxygen that little oxygen is available to tissues.” 2009, ISMP, 7(2)

FACTS

- Normally, methemoglobin is 1% of circulating hemoglobin.
- Cyanosis occurs as the level rises above 10%.
- Anxiety, fatigue, and tachycardia appear at 20% to 50%, and from 50% to 70%, coma and death may result.
Background

- Hurricaine spray contains benzocaine which is known to cause methemoglobinemia. When induced by benzocaine, methemoglobinemia can result in life-threatening conditions.

- The risk of methemoglobinemia due to benzocaine increases with the number and duration of sprays administered. According to the Hurricaine package insert, a \( \frac{1}{2} \) second spray should be administered, which may be repeated once. However, acknowledging human performance limitations, no one can reliably estimate fractions of seconds or visualize how thickly the spray coats the throat.
Several years ago, the Institute for Safe Medication Practices (ISMP) identified and analyzed 132 cases of life-threatening benzocaine-induced methemoglobinemia from reports submitted to ISMP and the US Food and Drug Administration (FDA). The cases included 107 serious adverse events (81.1%) and 2 deaths (1.5%).

Topical benzocaine has also been linked to Sudden Infant Death Syndrome (SIDS). A case reported in the literature involved the death of a 4-month-old infant that was classified as SIDS but later found to be benzocaine toxicity and methemoglobinemia. Postmortem toxicology showed a methemoglobin level of 36%. The child received three times more ALLERGEN Ear Drops (5.4% antipyrine, 1.4% benzocaine) than prescribed on the day prior to his death.
Background

- Not all clinicians realize benzocaine in topical sprays is absorbed systemically. In most cases of methemoglobinemia, clinicians used multiple sprays of benzocaine-containing products, or sprays of longer duration than recommended.

- Some products that contain benzocaine are available without a prescription, so patients could also use too much spray, gargle too often with a liquid form, or even swallow it.
Who is at risk?

- Some patients may be predisposed to methemoglobinemia:
  - Infants less than 6 months of age.
  - The elderly with cardiac problems.
  - Patients with altered hemoglobin, such as G6PD deficiency or methemoglobin reductase enzyme deficiency.
  - Application of benzocaine products to inflamed areas, which absorb more drug, can also contribute to the problem.
Clinical Manifestations

- Prompt recognition and treatment can be challenging because elevations of methemoglobin can produce normal pulse oximetry readings.
- Drawing arterial blood for co-oximetry, to directly measure methemoglobin levels, is needed. The brown appearance of arterial blood is another clue.
Clinical Manifestations

- The occurrence of acute cyanosis during endoscopic procedures, such as bronchoscopy, may be due to airway obstruction, but another possibility is the induction of acute methemoglobinemia as a result of the topical anesthetic agent used prior to the procedure (e.g., benzocaine, lidocaine, prilocaine).

- Clues that methemoglobinemia is present in such settings include the development of cyanosis in the presence of a normal arterial pO2 and/or the presence of "chocolate brown blood" in the videoscopic field despite supplemental oxygen therapy. Several deaths have been attributed to this complication.
Rapid recognition, coupled with immediate infusion of methylene blue (MB), can be life-saving.

**Dosing for methylene blue:**
- 1-2mg/kg (up to a total of 50mg in adults, adolescents and older children) by slow IV push (over 5 - 10 minutes) with a 1% methylene blue solution. Repeat dose may be given at 1mg/kg in one hour as needed to control symptoms.
What can clinicians do?

- **Ask patients** who may receive topical anesthetics about their medical history to determine if risk factors for methemoglobinemia (e.g., G6PD deficiency) are present.

- **Have pharmacy apply warning labels** to remind nurses to avoid sprays of longer duration than recommended.

- **Use a metered-dose spray** product of 20% benzocaine if possible (check with pharmacy for availability), and avoid multiple sprays.

- **Document** the number and duration of sprays applied to keep track of the amount of drug administered.
What can clinicians do?

- **Consider methemoglobinemia** if cyanosis develops after application of topical anesthetics, even if pulse oximetry readings are normal.

- **Become familiar** with treating methemoglobinemia if you administer topical benzocaine.

- **Have supplemental oxygen** and methylene blue (given 1 to 2 mg/kg IV to enhance the oxygen-carrying capacity of hemoglobin) available where benzocaine sprays are used.

- **Warn patients** who use topical anesthetics at home (e.g., oncology patients, parents of teething infants and children) about methemoglobinemia.
source=see_link&sectionName=Acquired+methemoglobinemia&anchor=H13#H25


If you are done viewing the eLearning, you can now take the exam. (Located on the left side of screen.)