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Cetacaine-induced Acute Methemoglobinemia

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Cetacaine spray (cetacaine: 14% benzocaine, butyl aminobenzoate 2.0%, tetracaine HCL 2.0%, cetyl dimethyl ethyl ammonium bromide 0.005%, benzalkonium chloride 0.5%) is a topical anesthetic used by various types of medical practitioners, including gastroenterologists, bronchoscopists, and anesthesiologists. We present a case of acute cyanosis requiring tracheal intubation and mechanical ventilation secondary to cetacaine-induced methemoglobinemia.

CASE REPORT

A 73-yr-old man with unresectable esophageal carcinoma was seen in our outpatient clinic for esophagoscopy. The patient had an esophagoscopy 4 weeks ago for local radiation implants. Past medical history was significant for renal insufficiency and anemia. Previous esophagoscopies using topical lidocaine were performed without incident.

Topical cetacaine was sprayed for approximately 10 s to the posterior pharynx and esophagus. No other medication was administered. Within 5 min after spraying the area, during which time esophagoscopy was attempted, the patient became cyanotic and hypotensive. While breathing oxygen via a nasal cannula at 4 l/min, $p\text{H}_a$ was 7.34,

Paco_2 28 mmHg, PaO_2 179 mmHg, HCO_3 15 mEq/l, SaO_2 saturation 100%. Prior to receiving the arterial blood gas results, the trachea was intubated and the patient was admitted to the Intensive Care Unit. He was on Assist/Control ventilation, tidal volume 800 ml/breath, respirations 16 breaths/min, FiO_2 1.0. Arterial blood pressure 120/60 mmHg, heart rate 122 bpm, temperature 37° C. Except for marked cyanosis, the remainder of the physical examination was unremarkable. Arterial blood sample obtained through an indwelling radial artery catheter was dark and "chocolate brown" in color. Chest radiograph was clear. Electrocardiogram revealed a sinus tachycardia. Co-oximetry of the arterial blood (Corning 2500 co-oximeter) revealed a hemoglobin of 7.8 g/dl, SaO_2 51%, methemoglobin level 48.5%. Arterial blood gas analysis of same blood revealed a PaO_2 of 573 mmHg and SaO_2 of 100%.

Methylene blue, 2 mg/kg in a 1% solution was administered over 20 min. Complete resolution of cyanosis occurred within 15 min. Repeat co-oximetry revealed a methemoglobin level of 4.7%, SaO_2 94%. The trachea was extubated, and he was discharged from the Intensive Care Unit on the following day. The remainder of his hospital course was uneventful.

DISCUSSION

Acute methemoglobinemia has been observed following the use of several local anesthetics.^{1,2} First reported in 1956, methemoglobinemia occurred following the use of lidocaine for a dental extraction.³ Other commonly used local anesthetics such as prilocaine^{1,2} and benzocaine can also cause methemoglobinemia.^{1,2,4-10} Cetacaine aerosol spray contains benzocaine 14.0%. Additionally, methemoglobinemia can be caused by exposure to oxidant drugs such as amines, phenols, nitrates, and aniline dyes.^{5,11}

The diagnosis of acute methemoglobin should be suspected in any patient who has received topical anesthesia

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and has become suddenly cyanotic. An arterial blood gas that is "chocolate brown" in color with a normal PaO_2 suggests this diagnosis. Standard blood gas determinations do not measure SaO_2 , but, rather, report a derived value based on pH_a and PaO_2 . Co-oximetry of arterial blood accurately identifies this condition, because SaO_2 is measured rather than calculated. The co-oximeter measures the absorbance of seven specific wavelengths through a film of the sample, thereby analyzing specific hemoglobin derivatives oxyhemoglobin, deoxyhemoglobin, methemoglobin, and carboxyhemoglobin. Treatment of methemoglobinemia is with 1–2 mg/kg of methylene blue (tetramethyl-thionine chloride) over 5 min.

Clinical cyanosis occurs when methemoglobin levels exceed 1.5 g/100 ml (10% of the total hemoglobin). At methemoglobin levels of $\geq 35\%$, patients experience weakness and a marked cyanosis.⁵ The methemoglobin molecules can disassociate into dimers, which then reassociate with nonoxidized dimers to form half-oxidized, hybrid tetramers. The tetramers have increased oxygen affinity and subsequently shift the oxygen-hemoglobin dissociation curve to the left, thereby less readily releasing oxygen to the tissues.¹²

Pulse oximetry can be an effective adjunct in diagnosis of this condition, revealing a low oxygen saturation. The pulse oximeter functionally discerns between oxyhemoglobin and deoxyhemoglobin by measuring the absorbance of light at two specific wavelengths, 660 nm and 925 nm. The percent of oxyhemoglobin and deoxyhemoglobin is proportional to the ratio of absorption of light at these two wavelengths. Other hemoglobin pigments, if present, are not recognized specifically but, rather, alter the calculated ratio based on its absorption spectrum. Furthermore, oxygen saturation appears to further decrease with pulse oximetry as treatment with methylene blue begins.^{12,13}

This patient demonstrates one of the highest methemoglobin level reported from exposure to cetacaine or any other local anesthetics. Factors that may increase the risk of topical anesthetic-induced methemoglobinemia are longer than recommended spraying time (>1 s), a decreased oxygen carrying capacity (low Hb), and a denuded, inflamed mucosal surface. All of these were present in this patient.

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