IATROGENIC METHEMOGLOBINEMIA FROM BENZOCAINE SPRAY IN TRAUMA

To the Editor:—Acquired methemoglobinemia is frequently reported in the literature, but rarely in association with trauma in which new-onset cyanosis might present a more confounding picture, particularly in association with traumatic injuries to the cardiopulmonary system. An understanding of the physiology and causes of methemoglobinemia will hasten its diagnosis, enable timely treatment, and thus potentially prevent needless morbidity.

A 64-year-old man presented to our trauma center after a fall of 16 feet from a roof. He suffered a head injury, open mandible fracture, and an open fracture dislocation of the left elbow. On arrival, the patient was felt to require endotracheal intubation.

During preoxygenation with 100% oxygen, peripheral saturations were 98% by finger probe. Wanting to avoid airway collapse with paralytic agents, we elected to pursue an awake oral intubation using etomidate and topical anesthetics. Benzocaine spray was thus applied to the posterior pharynx. Shortly after administration of the benzocaine pulse oximetry (SpO_2) decreased to 80% and cyanosis was visible on the lips and tongue. The cyanosis did not respond to further oxygenation, and chest auscultation remained normal. Concerned with progressive airway obstruction, we completed the oral intubation with some anxiety, but without difficulty. Despite oxygenation through a endotracheal tube with 100% oxygen, pulse oximetry remained near 80%.

An arterial blood gas was collected and revealed the following: pH 7.40, PaO_2 237 mm Hg, $PaCO_2$ 43 mm Hg, calculated SaO_2 77.0%, methemoglobin 21.0%. Hemoglobin level was 8.1 g/dL. The methemoglobinemia was recognized as the result of benzocaine and treated with methylene blue.

Methemoglobin (MHb) describes the oxidized form of the iron moiety (Fe3+) within the hemoglobin molecule. MHb is formed in the presence of an oxidizing substrate and is useless for delivering oxygen to the tissues at the cellular level. MHb is continuously formed and then reduced to the ferrous (Fe2+) hemoglobin in the body. Under normal physiology, MHb exists in concentrations of less than 1%. The cytochrome-b5-MHb reductase system is responsible for the vast majority of MHb reduction.

MHb is formed in excess through the ingestion of exogenous toxins, systemic acidosis, dietary intake of oxidizing substances, and genetic causes.[1-3]. Exposure to exogenous oxidizing toxins is the most commonly encountered cause. Some of these agents directly oxidize hemoglobin to the ferric state, whereas others act indirectly creating oxygen-free radicals that subsequently oxidize hemoglobin. There is wide variability in individual susceptibility to toxin-induced MHb, that is, not every person exposed to oxidizing agents will develop significant methemoglobinemia. Common causative medications include dapsone, phenazopyridine, nitrates, nitrites, naphthalene, and the anesthetics benzocaine, bupivacaine, and lidocaine.[1,2]

Clinical cyanosis resulting from MHb becomes apparent at a level of 1.5 g/dL. In a healthy individual, this usually corresponds to an MHb of 15% of total hemoglobin. MHb levels between 20% and 30% will often cause headache, tachycardia, and anxiety, whereas levels above 30% will frequently cause alterations in consciousness. MHb levels of greater than 70% are typically fatal. The clinical effect of methemoglobinemia can be magnified by the concurrent presence of anemia, like in our patient. As noted by Wright et al., a patient with a hemoglobin of 15 g/dL and a MHb level of 20% has a functional hemoglobin level of 12 g/dL, whereas a patient with a hemoglobin of 8 g/dL and 20% MHb has a functional hemoglobin level of only 6.4 g/dL.[1]

Because of limitations inherent to the devices, and the absorption wavelengths of the various hemoglobin forms, oximeters cannot measure the percentage of MHb in the blood and could provide inaccurate SpO_2 values when MHb is present.[4] A low pulse oximetry value, however, in the presence of cyanosis that does not respond to oxygen therapy, should suggest the presence of dysfunctional hemoglobin—most commonly MHb.[1] Arterial blood gas analysis using co-oximetry with spectroscopy will be diagnostic of MHb. The qualitative presence of methemoglobinemia can also be confirmed by simple bedside tests using potassium cyanide or oxygen.[1]

Intravenous methylene blue remains the standard treatment for symptomatic MHb. Methylene blue is metabolized to leukomethylene blue, which serves as a reducing agent for MHb. Because glucose-6-phosphate dehydrogenase (G6PD) is required to convert the oxidizing methylene blue to its reducing metabolite, persons with G6PD deficiency are at risk for complications of methylene blue therapy, including hemolysis and paradoxically increased MHb levels.[1,2] The administration of methylene blue will further interfere with accurate SpO_2 readings. Therefore, SpO_2 should be ignored following methylene blue administration.[4]

As EPs acquire increasing facility with advanced airway techniques, methemoglobinemia resulting from topical anesthetics could become more common. The rapid onset of cyanosis in a traumatically injured patient with an airway or breathing abnormality during an intubation procedure will present a more confusing clinical picture compared with more controlled settings. Familiarization with the causes and treatment of MHb will certainly help in these instances.

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References

1. Wright RO, Lewander WJ, Woolf AD: Methemoglobinemia: etiology, pharmacology, and clinical management. Ann Emerg Med 1999;34:646-656
2. Rehman HU: Methemoglobinemia. West J Med 2001;175:193-196
3. Griffey RT, Brown DF, Nadel ES: Cyanosis. J Emerg Med 2000;18:369-371
4. Sinex JE: Pulse oximetry: principles and limitations. Am J Emerg Med 1999;17:59-67

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STRESS REACTIONS AND ISCHEMIC CVAs AFTER THE SEPTEMBER 11, 2001 TERRORIST ATTACKS

To the Editor:—After the tragic events of September 11 in New York, many stress reactions have been reported. In particular, a study conducted by the University of California reported that after terrorist attacks, the 44% of adults who were not present at those events developed substantial symptoms of stress.[1] Furthermore, severe psychologic trauma and related stress can alter mental and physical healthness,[2,3] and the recent Caerphilly Study showed that psychologic distress has been associated with fatal ischemic strokes.[4]

We evaluate, from our register of acute cerebrovascular accidents, whether this circumstance led to an increase in ischemic cerebrovascular events.

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