

# METHEMOGLOBINEMIA WITH THE USE OF BENZOCAINE SPRAY FOR AWAKE FIBEROPTIC INTUBATION

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## Abstract

We report a case in which the use of benzocaine spray to facilitate awake fiber optic intubation (FOI) in a patient with a difficult airway caused methemoglobinemia intraoperatively. Local benzocaine was sprayed to numb the patient's airway for a total time of one second. fifteen minutes later SpO2 decreased to 85% on the pulse oximeter. Arterial blood gas (ABG) showed a MetHb of 24.6% of total Hemoglobin. The patient was successfully treated with methylene blue intravenously and recovered uneventfully. Small amounts of local benzocaine sprayed to numb the airway can cause significant methemoglobinemia that requires immediate recognition and appropriate management.

## Introduction

Benzocaine spray is commonly used to numb the airway for awake fiber optic intubations. It can cause significant methemoglobinemia, which usually occurs 15-20 minutes after its application, at that time the patient is usually under anesthesia covered with drapes. Many factors may drive the anesthesiologist away from promptly identifying methemoglobinemia which may delay treatment and have detrimental consequences on the patient. we report a case of methemoglobinemia under general anesthesia caused by benzocaine spray used for an awake fiberoptic intubation. We discuss diagnostic clues that help the anesthesiologist identify and manage methemoglobinemia as it occurs.

## Case Report

A 32 year old female patient with a large facial arteriovenous malformation scheduled for face reconstruction, laser treatment of the soft palate and Botox injection. She had history of twelve facial surgeries, in ten of which she had awake fiber optic intubations (FOI) without any complications due to anticipated difficult airway with her facial deformity and decreased mouth opening. On the morning of surgery, her vital signs were stable and her physical exam was normal. We anticipated a difficult airway and decided to proceed with awake fiber optic intubation. To facilitate the awake FOI and ensure patient's comfort we premedicated her with midazolam 2 mg IV, fentanyl 50

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mcg IV, and glycopylorate 0.2 mg IV. To anesthetize the airway we used cotton tip swaps to apply viscous lidocaine on the tonsillar pillars, lidocaine nebulizer 120 mg, lidocaine atomizer 80 mg, and sprayed benzocaine 20% (Hurricane) for 1 second. Awake FOI went smoothly. Anesthesia was induced smoothly with IV propofol. Vital signs remained stable during induction with SpO<sub>2</sub> around 97%. However, 15 minutes after induction we noticed bluish brown discoloration of the fingers and lips and SpO<sub>2</sub> went down to 85%, other vital signs remained stable. We increased FIO<sub>2</sub> to 100% and ensured adequate ventilation, however SpO<sub>2</sub> remained 85%. An arterial blood gas (ABG) showed a pH 7.5, pCO<sub>2</sub> 31, pO<sub>2</sub> 608, HCO<sub>3</sub> 22.8 on 100% O<sub>2</sub>. However, despite a pO<sub>2</sub> of 608, SpO<sub>2</sub> was 85%, we suspected methemoglobinemia based on the saturation gap. A second ABG with co-oximetry showed a pH 7.49, pCO<sub>2</sub> 31, pO<sub>2</sub> 323, HCO<sub>3</sub> 23.4, THb 10.6, O<sub>2</sub> Hb 74.5%, CoHb 0.3% and MetHb 24.6% on 100% O<sub>2</sub>. Based on the high MetHb level a diagnosis of methemoglobinemia was established. We treated the patient with methylene blue 2 mg/kg IV. SpO<sub>2</sub> went up to 95%. ABG after methylene blue showed a pH 7.49, pCO<sub>2</sub> 31, pO<sub>2</sub> 299, HCO<sub>3</sub> 23, THb 10.1, O<sub>2</sub> Hb 90.3%, CoHb 0.3% and Met Hb 9% on 100% O<sub>2</sub>. The patient remained stable throughout the

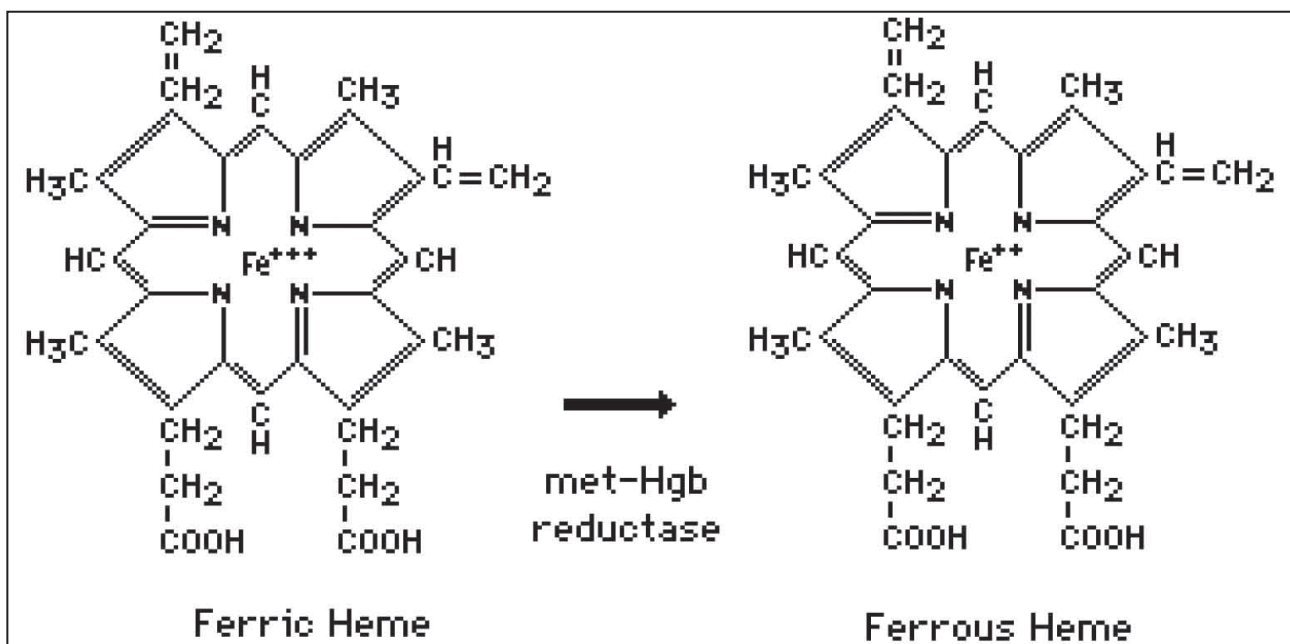
procedure. At the end, she woke up and was extubated without complications. Her postoperative course was uneventful.

## Discussion

Methemoglobin (MetHb) is an abnormal form of hemoglobin (Hb) that has a diminished capacity for carrying oxygen. It is produced when Hb is oxidized and an electron is removed from one of the iron atoms of the heme group causing the conversion of ferrous or Fe<sup>2+</sup> iron to the ferric or Fe<sup>3+</sup> state which diminishes the Hb molecule ability to bind O<sub>2</sub> causing a functional anemia (Fig. 1). It also results in a left shift of the oxygen-hemoglobin dissociation curve<sup>1</sup>. This in turn, depending on the level of MetHb, may cause cellular hypoxia and, ultimately, death.

The red blood cells are continuously subjected to oxidative stressors that result in the formation of methemoglobin spontaneously in normal individuals at a rate of 0.5-3% of the available hemoglobin per day. Reduction of methemoglobin maintains a steady state level of methemoglobin of about 1% of total hemoglobin. There are 2 mechanisms by which erythrocytes reverse the effects of oxidation and the formation of MetHb. The most significant of these

Fig. 1



is via nicotine adenine dinucleotide methemoglobin reductase (NADH-MetHb reductase), also known as cytochrome-b5 reductase<sup>2</sup>. The second, and less physiologically significant, is via NADPH-MetHb reductase. This second pathway requires a cofactor or an electron acceptor such as methylene blue or flavin to carry out the reduction of MetHb to Hb (Fig. 2). Individuals with a deficiency of NADH-MetHb reductase have insufficient enzyme levels for reduction of methemoglobin to occur and develop hereditary methemoglobinemia. They are particularly susceptible to worsening methemoglobinemia in the presence of oxidizing agents.

Medications are the most common cause of MetHb in clinical practice, of these, local anesthetics (benzocaine and procaine), antibiotics (dapson), and nitrites (nitroglycerin/nitric oxide) are the most common offenders.

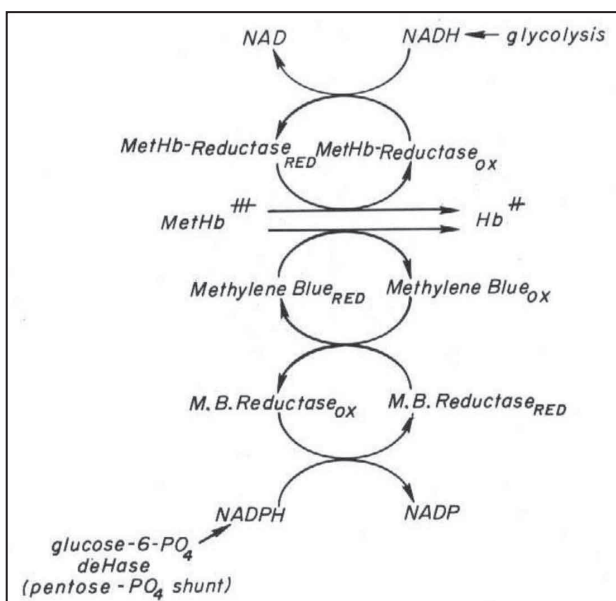
Benzocaine is one of the most powerful oxidizing agents among local anesthetics, animal studies showed it has a more powerful oxidizing effect than lidocaine, and a dose response relationship has been demonstrated between benzocaine and methemoglobin. Since 1977, when the first case of benzocaine spray induced methemoglobinemia was reported<sup>3</sup>, approximately 200 cases have been documented in the literature. Benzocaine has been

reported to cause methemoglobinemia when applied to infants as an ointment or a rectal suppository<sup>4,5</sup> and when used topically to the perineal area<sup>6</sup>. It has also been associated with methemoglobinemia after its use as a lubricant on endotracheal, bronchoscopic, and esophageal tubes<sup>7,8</sup>. The particular preparation of benzocaine spray used in this case contained benzocaine 20% (Hurricane), It is most often used prior to procedures such as endotracheal intubation, upper gastrointestinal endoscopy and transesophageal echocardiography.

Clinical findings are the first clue for the anesthesiologist to suspect methemoglobinemia, Low SpO<sub>2</sub> and cyanosis that fail to improve with increased inspired oxygen concentration, chocolate-colored, brown, blue, or black blood that fails to change color when exposed to air, and a discrepancy between SpO<sub>2</sub> and SaO<sub>2</sub> on ABG (saturation gap). However, co-oximetry is the diagnostic test of choice. Limitations of traditional pulse oximetry, which can detect only 2 wave lengths of ultraviolet light: 660 and 960 nm, leads to an unreliable measure of oxygen saturation, as a result, co-oximetry detecting multiple ultraviolet wavelengths and all four types of hemoglobin should be used to measure an arterial blood gas and confirm the diagnosis of methemoglobinemia<sup>9</sup>.

Treatment starts with discontinuing the offending agent, in most cases methemoglobinemia resolves within 24-36 hours after the clearing of the residual benzocaine. General supportive measures (O<sub>2</sub>, close observation) are appropriate when methemoglobin level is less than 30%. In more severe cases, methylene blue in the dose of 1 to 2 mg/kg of 1% solution, slow IV push over 5 minutes, is the preferred treatment. Methylene blue, along with NADPH, serve as cofactor for the enzyme NADPH-MetHb reductase<sup>4</sup>, This reaction contributes minimally to the reduction of methemoglobin under normal, physiologic conditions. However, if the normal reductive pathways are overwhelmed, as in methemoglobinemia, this pathway becomes very important. Methylene blue will cause marked reduction in the methemoglobin concentration, usually by 50%, within 30 to 60 minutes. Administration can be repeated in 1 hour if symptoms do not resolve.

Fig. 2



## Conclusion

Benzocaine spray is commonly used to numb the airway before awake FOI, it is associated with the risk of causing methemoglobinemia even when

used in small doses. We recommend avoiding the use of benzocaine spray before awake FOI. If used, the anesthesiologist should monitor the patient closely, look for signs of methemoglobinemia, and be prepared to treat it.

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