Case Report: Methemoglobinemia Caused by Benzocain Spray – A Warning for Surgeons

Abstract
Methemoglobinemia due to topical Benzocaine spray is an entity that has been well described in the literature, however it is quite uncommon. Many physicians use benzocain spray for patient comfort during and after several procedures, the most common being Transesophageal Echocardiography, Upper Endoscopy, Bronchoscopy, and Nasogastric Tube Placement. This condition is a potentially catastrophic one, especially if not considered, and diagnosed late. Methemoglobinemia should be considered in any patient who has oxygen resistant cyanosis, or an oxygen “saturation gap” between pulse oximetry and arterial blood gas, particularly if they are known to have had exposure to one of the substances that cause the condition. Herein we present a case of acquired methemoglobinemia, and a discussion of the pathophysiology, diagnosis and treatment.

Keywords: Methemoglobinemia; Surgery; Benzocaine; Topical anesthetic

Introduction
Methemoglobinemia is a condition whereby there is an increase in the fraction of methemoglobin in the red blood cells. The normal state of hemoglobin contains the iron molecule in the divalent ferrous state. Methemoglobin results from the oxidation of ferrous iron to a trivalent ferric iron. Methemoglobin cannot bind and carry oxygen. The outcome of this is a functional hypoxia due to the decreased oxygen carrying capacity of the red blood cells. Also, the remaining heme groups, which do not have the oxidized iron have an increased binding affinity for oxygen [1,2]. Therefore they do not release oxygen as easily at the tissue level and cause tissue hypoxia. As red blood cells are constantly exposed to oxidizing agents methemoglobin is formed at a rate of about three percent per day. Several physiologic mechanisms reduce it to deoxyhemoglobin. These pathways include the cytochrome b5, nicotinamide adenine dinucleotide (NADH), ascorbic acid, glucose-6-phosphate dehydrogenase (G6PD), and glutathione reduction enzyme systems. Under normal physiologic circumstances these mechanisms maintain equilibrium where the methemoglobin level is less than one percent [2].

Acquired Methemoglobinemia can be caused by a host of substances. Most commonly it is reported after the use of oropharyngeal topical anesthetic sprays such as Benzocaine, Lidocaine, and Prilocaine; Benzocaine is by far the most common. This results in elevated methemoglobin by direct or indirect oxidation of the hemoglobin [3]. Patients with methemoglobinemia may present with headaches, lack of energy, increased heart rate, shortness of breath, or light headedness. Signs that are present include cyanosis, dark brown discoloration of the blood, and low pulse oximetry in the presence of normal arterial blood gas readings [2,4]. Symptomatology has been correlated with methemoglobin levels. Levels in the ten percent to twenty-five percent range show cyanosis. Levels from thirty-five percent to forty percent cause headache, fatigue, dizziness and dyspnea. Levels of sixty percent can lead to arrhythmias, seizures, lethargy, and stupor. Levels greater than seventy percent have been associated with vascular collapse and death [5].

Treatment is generally begins with discontinuation of the offending agent. Not all acquired methemoglobinemia requires additional treatment. Usually if the methemoglobin level is less than twenty percent and the patient is asymptomatic no treatment is required. Generally if the methemoglobin level is greater than thirty percent, or there is cyanosis or respiratory or cardiac distress, the patient should be treated [5,6]. In the most severe cases, exchange transfusion or hyperbaric oxygen has been used with anecdotal success [6]. The treatment of choice for most cases is Methylene Blue, it provides an artificial electron transporter to aid in the reduction of methemoglobin. It is given in a dose of 1-2 mg/kg IV over five minutes [1]. Risks associated with Methylene Blue are as follows: Overdoses occur with doses larger than seven mg/kg, which can be cumulative from multiple administrations. Overdose can lead to dyspnea, chest pain, and hemolysis in certain individuals [7,8]. In patients with G6PD deficiency, Methylene Blue will likely be ineffective, and may lead to hemolysis [9].

Case Presentation
Our patient is an eighty-one year old female who presented with an adhesive small bowel obstruction. She was admitted to the hospital and had a short course of non-operative management. She continued to be obstipated and the decision was made to proceed to surgery. She underwent an abdominal exploration, and lysis of adhesions. Post operatively she had a nasogastric tube in place; she was given Benzocaine 20% spray topically for discomfort from the tube. After two applications she began to exhibit signs of cyanosis and her pulse oximetry reading fell to eighty-two percent.
percent, she had no respiratory difficulties. An arterial blood gas was obtained and the saturation was ninety-seven percent, at this time a methemoglobin level was obtained and it was 22%. The patient received 1mg/kg of Methylene Blue IV, six hours after this her cyanosis was gone, her saturation was 94% and her methemoglobin level was 8%, an additional methemoglobin level was obtained six hours later and it was three percent (Table 1).

| Methemoglobin Level (%) | Pulse Oximetry (%) | Arterial Blood Gas O2 Saturation (%) | Cyanosis | Methylene Blue given |
|-------------------------|--------------------|-------------------------------------|----------|---------------------|
| 22                      | 82                 | 97                                  | Yes      | 1mg/kg              |
| 8                       | 94                 | 98                                  | No       | None given          |
| 3                       | 96                 | 97                                  | No       | None given          |

**Table 1: Patient response to treatment.**

**Discussion**

Methemoglobinemia is a potentially fatal condition that is acquired due to an adverse reaction to a medication. Prior to this event our group used topical benzocaine spray as needed for anyone with any oropharyngeal discomfort, and routinely for anyone with a nasogastric tube. Methemoglobinemia is extremely rare and the vast majority of patients who receive benzocaine spray will not develop this condition, however one must have a high index of suspicion in order to avoid delay in treatment and possibly a devastating outcome.

**References**

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