

Case Report

Spurious Hypoxia: Consideration of Hemoglobinopathies

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Abstract

The use of the pulse oximeter to estimate oxygen saturation has revolutionized monitoring capabilities in medicine. However, there can be circumstances in which there is a discordance between oxygen saturation measurements via pulse oximeter (SpO₂) and actual arterial oxygen levels (PaO₂). In these situations, there is a possibility the patient could have a variant hemoglobin as the etiology of this discordance. This finding is generally incidental, and the patients are asymptomatic. However, knowledge of these variants is crucial and may spare patients unnecessary medical investigations. In this case report, two patients with variant hemoglobins found to have low oxygen saturations via pulse oximeter are presented, both of who underwent extensive medical workup and prolonged hospital stays.

ABBREVIATIONS

SpO₂: Oxygen Saturation via pulse Oximeter; PaO₂: Arterial Oxygen Level; paO₂: Partial Pressure of Oxygen; ABG: Arterial Blood Gas

INTRODUCTION

The use of the pulse oximeter to estimate oxygen saturation has revolutionized monitoring capabilities in medicine, and in some realms is even referred to as the fifth vital sign [1]. Its use can alert healthcare professionals when something may have affected the cardio-pulmonary systems and prompt the need for further investigation. In pediatrics, the pulse oximeter is crucial because it does not require a blood draw which is likely to cause crying and/or breath-holding in children. This perturbation in respiratory pattern immediately changes the blood gas values, making accurate interpretation challenging. As a result, measurement of oxygen saturation via pulse oximeter (SpO₂) has become the universal measure of arterial oxygen levels (PaO₂).

However, there are well documented instances in which the use of these devices to measure oxygen saturation may not be accurate, including motion artifact, poor perfusion, venous pulsation and nail polish [2-5] (Table 1). In other unique situations, patients may be unexpectedly found to have low

oxygen saturation readings by pulse oximeter and yet have normal oxygen saturation levels when measured by arterial blood gas analysis. It's important to remember that pulse oximeter programming is based upon a normal oxygen-hemoglobin dissociation curve. Therefore, in the circumstance of discordance between SpO₂ and PaO₂ measurements, it's wise to consider the possibility of a variant hemoglobin as the cause. In most cases, this finding is usually incidental and the patients are otherwise healthy and asymptomatic. Therefore, knowledge of these variant hemoglobinopathies is crucial and may spare patients unnecessary medical investigations [3]. In this case report, we present two patients with variant hemoglobins found to have low oxygen saturations via pulse oximeter, both of whom underwent extensive medical workup and prolonged hospital stays.

Table 1: Potential Factors Affecting Pulse Oximetry Measurements.

| Intrinsic Factors | Extrinsic Factors |
|----------------------------------------------------------------|----------------------------------------------------|
| Hemoglobinopathies | Nail Polish |
| Methemoglobin | Calibration Assumptions |
| Carbon Monoxide Poisoning | Environmental interference – ie excessive movement |
| Low amplitude pulse – ie hypotension, hypovolemia, hypothermia | |

CASE PRESENTATION

Case report 1

A 7 year old previously healthy male presented to an outside clinic with a one-week history of cough. On initial evaluation, he was found to be hypoxic with an oxygen saturation in the 80% range obtained via pulse oximeter. He was seen by his pediatrician, and a chest x-ray was obtained after confirming the SpO₂ reading. The chest x-ray was reportedly normal. Lung examination was also documented as normal. An arterial blood gas (ABG) was done and showed a partial pressure of oxygen (paO₂) of 93 mmHg. Hemoglobin electrophoresis was obtained in the office with results pending. After persistent low SpO₂ readings were obtained, the patient was referred to our hospital for further workup. The patient was admitted and ultimately had a three-week hospitalization for workup of this hypoxia. During this time, he remained asymptomatic, denying shortness of breath, chest pain, or increased work of breathing. Respiratory and cardiovascular examination remained normal. The patient was initially admitted to the pediatric intensive care unit for the hypoxia. He had some minimal improvement of his SpO₂ readings on 8L of supplemental oxygen via facemask. During his hospitalization, he had multiple chest xrays, a chest CT scan, pulmonary function tests, and echocardiogram performed, all of which were normal. The patient had consultations with pulmonology and cardiology. A respiratory viral panel was obtained and was positive for human metapneumovirus and *mycoplasma pneumoniae*. The patient was treated for atypical pneumonia with no improvement in oxygen saturations. An arterial blood gas analysis was done which showed a paO₂ of 93 mmHg and an oxygen saturation of 98%.

When the patient's oxygen saturations via pulse oximeter did not improve following macrolide therapy, he was presumed to have macrolide-resistant mycoplasma infection and was treated with a ten-day course of clindamycin. The results of the hemoglobin electrophoresis done by the patient's primary care physician returned during his hospitalization showing a hemoglobin variant. The patient remained asymptomatic despite persistent hypoxia measured by pulse oximeter and was discharged home with 0.5L supplemental oxygen to use at night. He had follow up as an outpatient with pediatric hematology. Hemoglobin cascade testing was sent to Mayo Clinic to confirm the presence of the hemoglobin variant and results showed 24% hemoglobin Aalborg. The nighttime supplemental oxygen was discontinued. The patient continues to do well despite incidental low oxygen saturations on pulse oximetry.

Case report 2

A 7-year-old male with a past medical history of hereditary spherocytosis status post splenectomy at age 3 years presented to an outside hospital following a head injury with a posterior scalp laceration. Upon arrival routine vital signs were measured, and the patient was found to have an oxygen saturation reading of 78% on pulse oximetry. The patient was otherwise asymptomatic. He was placed on 6L of supplemental oxygen via facemask with an increase of the oxygen saturation to only 84%. Given the concern for the hypoxia, which was minimally responsive to supplemental oxygenation, the patient was air flighted to our

facility. During his hospitalization, he had an echocardiogram and spiral chest CT done which were both normal. An arterial blood gas was obtained and showed a paO₂ of 116 mmHg and an oxygen saturation of 98%. The patient continued to look well clinically and remained asymptomatic with normal lung and cardiovascular examinations. Hemoglobin variants were sent and were reported as 17.8% "other hemoglobin". He continued to do well and was discharged home with close follow up with outpatient pediatric hematology. At his outpatient follow up visit, hemoglobin cascade testing was sent to Mayo Clinic and returned as 9.6% hemoglobin Sabine. The patient was lost to follow up but at that visit remained healthy and asymptomatic with normal exercise tolerance.

DISCUSSION

When patients present with low oxygen saturation readings, it generally causes a lengthy list of possible etiologies to flood the mind of the healthcare provider. From pulmonary to cardiovascular to infectious disease, the list can be quite extensive. However, in certain situations, the clinical presentation of the patient may be discordant with the readings obtained on pulse oximetry.

The modern pulse oximeter has been in use since the mid 1970's and has become an essential tool in estimating oxygen saturations in patients [5]. Its use can provide real-time, non-invasive assessments of patients oxygenation status. However, while incredibly useful, the accuracy of these machines may be limited in certain circumstances, particularly in cases where the clinical appearance of the patient does not correlate with the readings. Carboxy- and decarboxy-hemoglobin have differing light absorption patterns. A pulse oximeter measures this absorbance by using 2 diodes transmitting light of differing wavelengths across a tissue to measure the intensity of the wavelengths at the other side. The percent oxygen saturation of hemoglobin can then be derived using the known absorbance spectra of oxygenated and deoxygenated hemoglobin [5,6]. In the presence of a hemoglobinopathy, pulse oximetry alone may not be reliable to accurately measure oxygen saturation. In these circumstances, the hemoglobin molecule is altered often as a result of an amino acid substitution that changes the molecule's affinity for oxygen.

In the first case reported above, the patient was found to have hemoglobin Aalborg. This rare hemoglobin variant is the result of an arginine residue replacing glycine. As a consequence, this unstable hemoglobin has a decreased oxygen affinity. These patients in general are asymptomatic and are not associated with any severe hematological abnormality [7]. The second case presented is the result of hemoglobin Sabine. This unstable hemoglobin is the result of a leucine residue being substituted for proline. This substitution causes disruption of the heme pocket and weakens the heme-globin bonding leading to a reduced affinity for oxygen molecules. Unlike the patient of case #1, patients with hemoglobin Sabine tend to have a higher degree of anemia as a result of hemolysis secondary to the instability of this hemoglobin molecule. The patient of this case received the diagnosis of spherocytosis at another facility. Repeat osmotic fragility testing done at our institution was normal, making it likely that the patient's previous symptoms of hemolytic anemia

were in fact due to the presence of the hemoglobin Sabine and not a result of spherocytosis [8].

Though hemoglobinopathies are relatively rare, the knowledge of their existence is crucial. There are hundreds of hemoglobin variants that have been identified to date. The affinity of the molecule for oxygen differs among the multitude of hemoglobin variants. Some variants may cause hemolytic anemia due to their instability. Others cause methemoglobinemia, cyanosis or polycythemia as a result of their increased oxygen affinity. And then there are those with a decreased oxygen affinity that often show no clinical symptomatology [9]. Both of the examples presented here have a lowered affinity for oxygen. Many of these patients are asymptomatic and are incidentally found to have low oxygen saturations via pulse oximeter, though further investigation shows normal partial pressure of oxygen in the arterial blood. These patients tend to do quite well and are not truly hypoxic, as the pulse oximeter may read.

Though the use of pulse oximetry has greatly advanced our monitoring abilities in medicine, it's important to recognize its limitations. Several studies exist that document the lack of knowledge of these limitations among many health care professionals [10-12]. When asymptomatic patients present with low SpO₂ readings via pulse oximetry and no clinical evidence to support the finding, the PO₂ should be measured and consideration of a hemoglobinopathy as a potential etiology is warranted. Though rare, knowledge of these diagnoses has the potential to spare patients unnecessary medical interventions and prolonged hospitalizations.

In pediatrics, the pulse oximeter is crucial because it does not require a blood draw, which is likely to cause crying and/or breath-holding in children. This perturbation in respiratory pattern immediately changes the blood gas values, making accurate interpretation challenging. As a result, SpO₂ has become the universal measure of PaO₂, despite these potential pitfalls.

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