Pseudohypoxemia: interpretation of discrepancies between SaO₂ and SpO₂

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ÖZET
Psödohipoksemi: SaO₂ ve SpO₂ arasındaki uyumsuzlukların yorumu


Anahtar Kelimeler: Hipoksemi, pulse oksimetri, psödohipoksemi, kronik lenfositik lösemi.

SUMMARY
Pseudohypoxemia: interpretation of discrepancies between SaO₂ and SpO₂

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Pulse oximetry is an important tool in evaluation and management of patients with cardiopulmonary disease. It provides an accurate, continuous, non-invasive measurement of oxygenation, however it has some limitations. Pseudohypoxemia is an artifactual condition that has been reported in patients with extreme leukocytosis and thrombocytosis. It should be suspected in patients with a discrepancy between oxygen saturation measured by pulse oximetry and that in arterial blood. High level of suspicion is needed to diagnose this condition as not doing so may lead to unnecessary escalation of therapy (i.e., increased levels of oxygen and mechanical ventilation). We provide a review of the principles and limitations of pulse oximetry and discuss the pathophysiology and diagnosis of pseudohypoxemia.

Key Words: Hypoxemia, pulse oximetry, pseudohypoxemia, chronic lymphocytic leukemia.

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We recently evaluated a 66 year-old man with history of chronic lymphocytic leukemia (CLL), ischemic heart disease and chronic obstructive pulmonary disease who presented with three-months history of progressive, exertional dyspnea associated with cough productive of yellow sputum. Two weeks prior to admission, he was noted to be hypoxicemic and started on supplemental oxygen at 2 liters per minute. The patient also had lost about 20 lbs of weight within the last year. Since CLL was unresponsive to chemotherapy, he was being managed with leukopheresis on as needed basis.

Physical examination revealed a thin, elderly man who was in mild respiratory distress. He was afebrile and had a blood pressure of 130/70 mmHg. His pulse was 84/min and regular and respiratory rate was 20 breaths/minute. Pulse oximetry (SpO2) revealed an oxygen saturation (SaO2) of 88% while breathing room air. The SpO2 increased to 92% on oxygen at 2 liters per minute. Significant findings on exam included bilateral axillary lymphadenopathies, 2 x 2 cm mass in the right breast, decreased breath sounds and vocal fremitus with dullness to percussion over lower one-third of the left lung. Few crackles were heard over upper half of the left lung while the right lung was clear. Examination of the heart was normal. Liver was palpable 3 cm below the costal margin with a liver span of 12 cm. The patient did not have clubbing, cyanosis or peripheral edema.

Chest radiograph showed widened mediastinum with pleural thickening on the left side. Computed tomography (CT) of the chest confirmed the presence of extensive mediastinal masses with extrinsic compression of left mainstem bronchus. Complete blood cell count revealed a white cell count of 282,000/mm³ (98% lymphocytes), a hemoglobin of 7.8 g/dL and a platelet count of 63,000/mm³.

As a part of initial work-up, an arterial blood gas (ABG) was obtained within 3 hours of admission. The results of ABG on 2 liters/minute of oxygen via nasal cannula were as follows: pH 7.38, PaCO2 47 mmHg, PaO2 31 mmHg and SaO2 54%. Increasing levels of supplemental oxygen failed to increase patient’s SaO2 above 60%. A repeat blood gas analysis on a non-rebreather mask was: pH 7.39, PaCO2 46 mmHg, PaO2 35 mmHg and SaO2 60%. While preparations for intubation were being made for management of hypoxicemic respiratory failure, the SpO2 was noted to be 99% on non-rebreather mask. A repeat ABG again showed pH 7.37, PaCO2 48 mmHg, PaO2 37 mmHg and SaO2 57%. There was no significant carboxyhemoglobinemia or methemoglobinemia. Interestingly, the patient did not show any signs of clinical deterioration or increasing respiratory distress on physical exam. He denied any worsening of his dyspnea since admission.

A repeat ABG on 2 liters/minute of oxygen was transferred on ice and processed within one minute. It showed a pH of 7.40, PaCO2 of 45 mmHg, PaO2 of 41 mmHg and SaO2 of 73%. Simultaneous SaO2 was again 92%. Another blood sample on 2 liters per minute of oxygen was obtained and immediately centrifuged to analyze partial pressure of oxygen in plasma. The results were as follows: pH 7.46, PaCO2 37 mmHg, PaO2 68 mmHg. The decision for intubation was deferred. Patient subsequently underwent bronchoscopy and endobronchial biopsy of an endobronchial mass in left mainstem, which showed non-small cell bronchogenic carcinoma. He was treated for possible post-obstructive pneumonia and discharged home on oxygen at 2 liters per minute after three days of hospitalization. Our experience with this case has led to the review of literature on pseudohypoxemia and the differential diagnosis of discrepancies between SaO2 and SpO2.

**Pulse Oximetry**

**Principles of Pulse Oximetry**

Pulse oximetry is a non-invasive technique that allows continuous monitoring of arterial oxygenation (1). Pulse oximetry utilizes spectrophotometric principles to determine O2 saturation of hemoglobin (2). It is based on the assumption that it is the arterial blood that is responsible for the only pulsatile absorbance between the light source and the photodetector. The light source in the oximeter probe has two light-emitting diodes that produce light at two different wave-
lengths, 660 nm (red) and 940 nm (infrared). The rationale for the use of these two wavelengths is the used different absorption spectra that oxyhemoglobin and reduced hemoglobin possess at these particular wavelengths. In the red region, oxyhemoglobin absorbs less light than does reduced hemoglobin, while the reverse is true in the infrared region.

**Limitations of Pulse Oximetry**

There are many factors that affect the accuracy of SpO₂, which diminishes with reductions in SaO₂. Most pulse oximeters have been reported to have 95% confidence limits of 4% for SaO₂ readings above 70% (3). Pulse oximetry is reasonably accurate and precise especially when SaO₂ is above 90%, however its accuracy decreases when SaO₂ falls below 80% (4,5).

There are many factors that influence the accuracy of SpO₂ readings (Table 1) (1). Pulse oximeters measure saturation, which is physiologically related to PaO₂ according to the oxyhemoglobin dissociation curve. Factors that shift the curve, such as temperature, pH and PaCO₂ affect the relationship between SaO₂ and PaO₂. Due to the sigmoid shape of the oxyhemoglobin dissociation curve, pulse oximetry is relatively insensitive detecting changes in PaO₂ at high levels of oxygenation. In the upper portion of the curve, large changes in PaO₂ may occur with little change in SaO₂.

Bright ambient light can also interfere with the accuracy of pulse oximetry, an effect that can be overcome with adequate shielding of the oximetry probe. Since oximetry readings depend on light absorption by Hgb, anemia thought to affect the accuracy of the equipment. However, pulse oximetry appears to be accurate in anemia without associated hypoxemia, but the combined effect of anemia and hypoxemia has yet to be determined. Dyes that are administered for therapeutic purposes and diagnostic studies (i.e. methylene blue, indocyanine green and indigo carmine) can cause falsely low SpO₂ readings (6). This effect is usually temporary and diminishes with the redistribution of the dye (6). Nail polish with colors that have absorbencies at the same wavelength used in the pulse oximetry (i.e., blue, green and black colors) can interfere with its accuracy (7).

**Discrepancies Between SaO₂ and SpO₂**

Although the accuracy of SpO₂ decreases at lower SaO₂ levels, the readings still remain relatively close within the limitations of the oximeters. There are several conditions that can lead to a discrepancy between SaO₂ and SpO₂. Among these conditions, hemoglobinopathies such as carboxyhemoglobin (COHgb) and methemoglobin (MetHgb) are often encountered in daily practice. Both COHgb and MetHgb have absorption characteristics in the same region of the spectrum as oxyhemoglobin (HgbO₂) and reduced Hgb and thus may affect the SpO₂ reading when present in significant amounts.

Carbon monoxide markedly influences the accuracy of pulse oximetry. COHgb consistently overestimates the true SaO₂. In one study, SpO₂ was found to be as low as 30% when SpO₂ was above 90% (8). Since the absorption coefficient of COHgb is similar to that of HgbO₂, the two-wavelength oximeter misinterprets COHgb as HgbO₂ and thus overestimates HgbO₂ content. The SpO₂ readings approximated the sum of COHgb and HgbO₂ (8).

MetHgb also results in inaccurate oximetry readings (9,10). SpO₂ readings overestimate true

<table>
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<th>Table 1. Factors that influence the accuracy of pulse oximetry.</th>
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<td>Shape of the oxygen dissociation curve</td>
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<td>Hemoglobinopathies</td>
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<td>Carboxyhemoglobin</td>
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<td>Methemoglobin</td>
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<td>Low-perfusion state (i.e., shock, vasoconstriction, hypothermia)</td>
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<td>Cardiac arrhythmias</td>
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<td>Anemia (sickle cell anemia)</td>
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<td>Nail polish (blue, green and black)</td>
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SaO₂ by an amount that is proportional to MetHgb until the MetHgb reached approximately 35% (10). SpO₂ values reach a plateau of about 85% at this level and do not decrease further despite an increase in MetHgb levels. This phenomenon arises because MetHgb has approximately the same absorption coefficient at both the red and infrared wavelengths. If the concentration of MetHgb is high enough, it dominates all pulsatile absorption and the pulse oximeter will measure the pulse-added absorbance ratio of these two wavelengths to 1.0, which corresponds to an SpO₂ value of about 85% on the pulse oximeter calibration curve (10).

**PSEUDOHYPOXEMIA**

Pseudohypoxemia is an artifactual phenomenon presenting with a significant gradient between oxygen saturation measured by SpO₂ and SaO₂ (11). It has been described in patients with very high leukocyte counts and those with thrombocytosis (11,12). It can result from consumption of oxygen by leukocytes and platelets, which account for most the oxygen consumed by whole blood. Interference of leukocytes with the O₂ electrode by coating the membrane and mechanically preventing the movement of the O₂ molecules from plasma into the O₂ electrode has been proposed as an alternative mechanism to explain the low PaO₂ in the presence of extreme leukocytosis (13).

Mature red cells do not contribute to the oxygen consumption as they lack mitochondria and therefore oxidative enzymes. Metabolic respiration of a leukocyte is about 45 times that of a platelet but since there are normally about 50 times more platelets than leukocytes per volume unit of blood, the contribution of these cells to oxygen consumption is quite similar. In patients with extreme leukocytosis, PaO₂ falls progressively due to consumption of oxygen by leukocytes (12). The rate of O₂ consumption and thus fall in PaO₂ decreases if the blood sample is stored in ice. The PaO₂ depends on the leukocyte count, the time delay between the collection of blood sample and the testing and the temperature at which the sample is stored. Type and maturity of leukocytes are other determinants of the rate of oxygen consumption. Monocytes have the highest rate of oxygen consumption. The rate of oxygen consumption by lymphocytes decreases as they mature (14,15). There is controversy on whether oxygen consumption in leukemic cells is higher than that in normal leukocytes (16,17).

For accurate measurement of PaO₂ and SaO₂ in cases of extreme leukocytosis or thrombocytosis, the blood sample should be placed in ice and analyzed as quickly as possible. As was the case in our patient, if interference of leukocytes with oxygen electrode is suspected, plasma may be used for measurement of partial pressure of oxygen.

**CONCLUSION**

Pulse oximetry is a useful technology that provides a relatively accurate and reliable, continuous monitoring capability of oxygenation non-invasively. However, there are a myriad of conditions that can affect its accuracy. Pseudohypoxemia is a rare condition that presents with a discrepancy between SpO₂ and SaO₂ and should be considered in the differential diagnosis of hypoxemia in cases of extreme leukocytosis or thrombocytosis. High level of suspicion is needed to diagnose this condition as not doing so may lead to unnecessary escalation of therapy (i.e., increased levels of oxygen and mechanical ventilation).

**REFERENCES**