Pseudohypoxemia: interpretation of discrepancies between SaO_2 and SpO_2

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ÖZET

Psödohipoksemi: SaO_2 ve SpO_2 arasındaki uyumsuzlukların yorumu

Pulse oksimetre kardiyopulmoner hastalığı olan hastaların değerlendirilmesi ve tedavisinde önemli bir araçtır. Bazı sınırlamaları olsa da, oksijenizasyonun noninvaziv, yeterli ve devamlı olarak ölçümünü sağlar. Psödohipoksemi, aşırı lökositoz ve trombositozu olan hastalarda bildirilen bir durumdur. Pulse oksimetre ile yapılan ölçüm ile arter kan gazında ölçülen oksijen satürasyonu arasında uyumsuzluk olan hastalarda bundan şüphe edilmelidir. Bu durumun tanısını koymak için şüphelenilmesi tedavinin arttırılmasını (oksijen düzeylerinin yükseltilmesi ve mekanik ventilasyon gibi) önlemek için gerekmektedir. Bu derlemede; pulse oksimetrenin prensipleri ve sınırlamaları, psödohipokseminin fizyopatolojisi ve tanısını tartışmaktayız.

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

SUMMARY

Pseudohypoxemia: interpretation of discrepancies between SaO_2 and SpO_2

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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 hypoxemic 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 an 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 (SpO_2) revealed an oxygen saturation (SaO_2) of 88% while breathing room air. The SpO_2 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/mm^3 (98% lymphocytes), a hemoglobin of 7.8 g/dL and a platelet count of 63.000/mm^3.

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, $PaCO_2$ 47 mmHg, PaO_2 31 mmHg and SaO_2 54%. Increasing levels of supplemental oxygen failed to increase patient's SaO_2 above 60%. A repeat blood gas analysis on a non-rebreather mask was: pH 7.39, $PaCO_2$ 46 mmHg, PaO_2 35 mmHg and SaO_2 60%. While preparations for intubation were being made for management of hypoxemic respiratory failure, the SpO_2 was noted to be 99% on non-rebreather mask. A repeat ABG again showed pH 7.37, $PaCO_2$ 48 mmHg, PaO_2 37 mmHg and SaO_2 57%. There was no significant carboxyhemoglobulinemia or methemoglobulinemia. 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, $PaCO_2$ of 45 mmHg, PaO_2 of 41 mmHg and SaO_2 of 73%. Simultaneous SaO_2 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, $PaCO_2$ 37 mmHg, PaO_2 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 SaO_2 and SpO_2.

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 O_2 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 SpO_2, which diminishes with reductions in SaO_2. Most pulse oximeters have been reported to have 95 confidence limits of 4% for SaO_2 readings above 70% (3). Pulse oximetry is reasonably accurate and precise especially when SaO_2 is above 90%, however its accuracy decreases when SaO_2 falls below 80% (4,5).

There are many factors that influence the accuracy of SpO_2 readings (Table 1) (1). Pulse oximeters measure saturation, which is physiologically related to PaO_2 according to the oxyhemoglobin dissociation curve. Factors that shift the curve, such as temperature, pH and $PaCO_2$ affect the relationship between SaO_2 and PaO_2. Due to the sigmoid shape of the oxyhemoglobin dissociation curve, pulse oximetry is relatively insensitive detecting changes in PaO_2 at high levels of oxygenation. In the upper portion of the curve, large changes in PaO_2 may occur with little change in SaO_2.

Table 1. Factors that influence the accuracy of pulse oximetry.

Shape of the oxygen dissociation curve
Hemoglobinopathies
Carboxyhemoglobin
Methemoglobin
Low-perfusion state (i.e., shock, vasoconstriction, hypothermia)
Cardiac arrhythmias
Anemia (sickle cell anemia)
Dyes
Nail polish (blue, green and black)
Ambient light
Motion artifacts
Skin pigmentation

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 SpO_2 readings (6). This effect is usually temporary and dimishes 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 SaO_2 and SpO_2

Although the accuracy of SpO_2 decreases at lower SaO_2 levels, the readings still remain relatively close within the limitations of the oximeters. There are several conditions that can lead to a discrepancy between SaO_2 and SpO_2. 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 ($HgbO_2$) and reduced Hgb and thus may affect the SpO_2 reading when present in significant amounts.

Carbon monoxide markedly influences the accuracy of pulse oximetry. COHgb consistently overestimates the true SaO_2. In one study, SpO_2 was found to be as low as 30% when SpO_2 was above 90% (8). Since the absorption coefficient of COHgb is similar to that of $HgbO_2$, the two-wavelength oximeter misinterprets COHgb as $HgbO_2$ and thus overestimates $HgbO_2$ content. The SpO_2 readings approximated the sum of COHgb and $HgbO_2$ (8).

MetHgb also results in inaccurate oximetry readings (9,10). SpO_2 readings overestimate true

SaO_2 by an amount that is proportional to MetHgb until the MetHgb reached approximately 35% (10). SpO_2 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 SpO_2 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 SpO_2 and SaO_2 (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 O_2 electrode by coating the membrane and mechanically preventing the movement of the O_2 molecules from plasma into the O_2 electrode has been proposed as an alternative mechanism to explain the low PaO_2 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, PaO_2 falls progressively due to consumption of oxygen by leukocytes (12). The rate of O_2 consumption and thus fall in PaO_2 decreases if the blood sample is stored in ice. The PaO_2 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 PaO_2 and SaO_2 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 noninvasively. However, there are a myriad of conditions that can affect its accuracy. Pseudohypoxemia is a rare condition that presents with a discrepancy between SpO_2 and SaO_2 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

1. *Jubran A. Pulse oximetry. In: Tobin MJ (ed). Principles and Practice of Intensive Care Monitoring. New York: McGraw-Hill, 1998: 261-87.*
2. *Tremper KK, Barker SJ. Pulse oximetry. Anesthesiology 1989; 70: 98-108.*
3. *Tobin MJ. Respiratory monitoring. JAMA 1990; 264: 244-51.*
4. *Nickerson BG, Sarkisian C, Tremper K. Bias and precision of pulse oximeters and arterial oximeters. Chest 1988; 93: 515-7.*
5. *Morris RW, Nairn M, Torda TA. A comparison of fifteen pulse oximeters. Part I: A clinical comparison; Part II: a test of performance under conditions of poor perfusion. Anaesth Intensive Care 1989; 17: 62-73.*
6. *Scheller MS, Unger RJ, Kelner MJ. Effects of intravenously administered dyes on pulse oximetry readings. Anesthesiology 1986; 65: 550-2.*

7. *Cote CJ, Goldstein EA, Fuchsman WH, Hoaglin DC. The effect of nail polish on pulse oximetry. Anesth Analg 1988; 67: 683-6.*
8. *Barker SJ, Tremper KK. The effect of carbon monoxide inhalation on pulse oximeter signal detection. Anesthesiology 1987; 67: 599-603.*
9. *Anderson ST, Hajduczek J, Barker SJ. Benzocaine-induced methemoglobinemia in adults: accuracy of pulse oximetry with methemoglobinemia. Anesth Analg 1988; 67: 1099-101.*
10. *Barker SJ, Tremper KK, Hyatt J. Effects of methemoglobinemia on pulse oximetry and mixed-venous oximetry. Anesthesiology 1989; 70: 112-7.*
11. *Hess CE, Nichols AB, Hunt WB, Suratt PM. Pseudohypoxemia secondary to leukemia and thrombocytosis. N Engl J Med 1979; 301: 361-3.*
12. *Gorski TF, Ajemian M, Hussain E, et al. Correlation of pseudohypoxemia and leukocytosis in chronic lymphocytic leukemia. South Med J 1999; 92: 817-9.*
13. *Charan NB, Marks M, Carvalho P. Use of plasma for arterial blood gas analysis in leukemia. Chest 1994; 105: 954-5.*
14. *Hedeskov CJ, Esmann V. Respiration and glycolysis of normal human lymphocytes. Blood 1966; 28: 163-74.*
15. *Pachman LM. The carbohydrate metabolism and respiration of isolated small lymphocytes. In vitro studies of normal and phytohemagglutinin stimulated cells. Blood 1967; 30: 691-706.*
16. *Bird RM, Clements JA, Becker LM. The metabolism of leukocytes taken from peripheral blood of leukemic patients. Cancer 1951; 4: 1009-14.*
17. *Laszlo J. Energy metabolism of human leukemic lymphocytes and granulocytes. Blood 1967; 30: 151-67.*