Pulse Oximetry Is a Poor Predictor of Hypoxemia in Stable Children With Sickle Cell Disease

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Objective: To evaluate the accuracy of the pulse oximeter to detect hypoxemia in patients with sickle cell disease in an ambulatory care setting.

Study Design: Simultaneous measurements of PaO₂, arterial oxygen saturation by co-oximetry (criterion standard), and pulse oximetry were performed in 21 children with sickle cell disease during 22 outpatient visits. The bias and precision of the pulse oximeter compared with measured arterial oxygen saturation by co-oximetry were determined. The sensitivity, specificity, and positive and negative predictive values of the pulse oximeter to detect hypoxemia (PaO₂ <70 mm Hg) were also calculated.

Results: The mean difference between pulse oximetry and measured oxygen saturation (bias) was 5.0% and the SD (precision) was 5.3. Twenty-one patients had a PaO₂ greater than 70 mm Hg; 7 of these (33%) were predicted to be hypoxic by pulse oximetry with values less than 93%, for a specificity to detect normoxia of 67%.

Conclusion: Making treatment decisions based on pulse oximetry data alone in patients with sickle cell disease who are not acutely ill may be inappropriate.


LUNG DISEASE in individuals with sickle hemoglobin is responsible for significant morbidity and mortality. Acute chest syndrome (ACS), characterized by fever and new infiltrates on chest radiograph, is the second most common cause of hospitalization in patients with sickle cell disease and causes 25% of deaths. Repeated episodes of ACS are associated with development of chronic lung disease, with progressive hypoxemia and decreased survival. Alternatively, hypoxemia may predispose to development of ACS.

Difficulties exist, however, in the evaluation of hypoxemia in patients with sickle cell anemia. Before the widespread adoption of pulse oximetry, PaO₂ by blood gas monitoring had been the standard for evaluating hypoxemia. The criterion standard for measuring arterial oxygen saturation (SaO₂) is analysis of an arterial blood sample by co-oximetry, which measures fractional SaO₂ (oxyhemoglobin as a proportion of total hemoglobin, including nonfunctional hemoglobins such as carboxyhemoglobin and methemoglobin). Although the co-oximeter was the criterion standard used to validate pulse oximeter devices in healthy populations, it is infrequently used clinically. In most clinical situations, oxygen saturation is not directly measured from an arterial blood sample but is calculated using a normal oxyhemoglobin dissociation curve from the PaO₂.

Pulse oximetry is a convenient, in vivo, noninvasive technique for measuring oxygen saturation. It combines the principles of spectrophotometry with those of photoelectric plethysmography to determine the oxygen saturation of hemoglobin. Oxygen saturation is determined by the ratio of oxyhemoglobin to the sum of oxyhemoglobin and reduced hemoglobin. Pulse oximeters perform optical measurements at only 2 wavelengths of light to discriminate oxygenated and deoxygenated hemoglobin. Carboxyhemoglobin and methemoglobin also absorb light at the wavelengths measured by the pulse oximeter and, if abundant, can affect the accuracy of the pulse oximeter. These devices were calibrated using healthy volunteers with insignificant amounts of dysfunctional hemoglobins.

Pulse oximetry is widely used to assess arterial oxygenation. It provides a useful estimate of hypoxia, in which oxygen...
PATIENTS AND METHODS

Twenty-one patients with documented sickle cell hemoglobinopathy (Hb SS only) were evaluated during routine outpatient visits (N = 22) to the Pediatric Hematology or Pulmonary clinics at Johns Hopkins Hospital, Baltimore, Md, an inner-city university teaching hospital, between March 1, 1992, and April 30, 1998. Patients were clinically well at the time of the study. Their ages ranged from 3 to 18 years (mean, 10.9 years); 9 were girls and 12 were boys. No patient was receiving long-term transfusion therapy. All measurements were made while the patient was breathing room air.

Oxygen saturations by pulse oximetry (SpO2) were recorded by one of us (K.C.) using a Criticare 504-US pulse oximeter (Criticare, Waukesha, Wis) after at least 2 minutes of stable SpO2 determined in the presence of a regular pulsatile photoplethysmography signal apparent on the visual display of the oximeter. Arterial blood samples were drawn in sterile fashion by the same skilled investigator (K.C.). Blood samples were transported on ice to a blood gas analyzer with a built-in co-oximeter (Radiometer ABL 520; Westlake, Ohio), and arterial oxygen saturation and blood gas analyses were performed within 10 minutes; SaO2, pH, PaCO2, and PaO2 values were recorded.

For each patient, we computed the difference between SpO2 and SaO2 and reported the frequency of distribution of these differences, the bias (mean difference between SpO2 and SaO2), and the precision (SD).

We also plotted SpO2 with PaO2 for each individual to determine the ability of pulse oximetry to detect hypoxemia. Low oxygen saturation was defined as less than 93% because this would predict a PaO2 less than 70 mm Hg based on a normal oxyhemoglobin curve. We chose this value because hypoxemia with a PaO2 less than 70 mm Hg has been associated with significant chronic lung disease and is associated with development of right ventricular hypertrophy in patients with sickle hemoglobin. To evaluate the accuracy of the pulse oximeter to detect hypoxemia, we determined the sensitivity (the percentage of patients with an SpO2 <93% and a PaO2 <70 mm Hg of all patients with a PaO2 <70 mm Hg), specificity (the percentage of patients with an SpO2 >93% and a PaO2 >70 mm Hg of all patients with a PaO2 >70 mm Hg), positive predictive value (the percentage of patients with a PaO2 <70 mm Hg of all patients with an SpO2 <93%), and negative predictive value (the percentage of patients with a PaO2 >70 mm Hg of all patients with an SpO2 >93%).

In this study of patients with sickle cell disease, the bias was 5.0% and the precision was 5.3. The difference between SpO2 and SaO2 was greater than 4% in 13 of 22 measurements >2 SD of the expected precision of 2.4,8 (Figure 1). Only 1 SpO2 measurement was more than 4% lower than the SaO2.

Twenty-one patients with 22 outpatient visits were normoxic by PaO2 (>70 mm Hg) (Figure 2). The reference oxyhemoglobin curve is presented for comparison. The oxyhemoglobin curve is shifted to the right in many patients with sickle cell disease, and there is wide variability. Only 14 measurements were predicted to be normoxic by pulse oximetry, so specificity of pulse oximetry was only 67% (95% confidence interval, 45%-86%). Because the incidence of hypoxia by blood gas analysis saturations of less than 93% predict a PaO2 less than 70 mm Hg. The pulse oximeter has been validated in various cohorts of patients with presumably “normal” hemoglobins, such as neonates, and patients with cyanotic heart disease. However, its validity in patients with hemoglobinopathies has not been evaluated, to our knowledge. The PaO2 at which the oxygen saturation is 50% (P50) is 26.5 mm Hg in individuals with normal hemo-
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Several studies have evaluated the accuracy of pulse
oximetry in patients with sickle cell anemia. One of the
first studied only 3 patients at the time of 4 hospitaliza-
tions. The authors concluded that pulse oximetry can be
used to detect the degree of shift of an oxyhemoglo-in curve for an individual with sickle hemoglobin, but
they did not describe its use as a tool to detect hypox-
emia (low PaO₂). Several investigators have com-
pared pulse oximetry to calculated arterial oxygen
saturations based on a normal P50 from a blood gas
sample. Although investigators have concluded that
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curve in sickle cell disease might have erroneously
affected the interpretations of both of these studies.

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Several investigators have attempted to correlate pulse
oximetry measurements with severity of disease. Pul-
se oximeters have been validated in healthy, nonsmoking
individuals and have an expected bias of 2% (mean differ-
ce between SpO₂ and SaO₂) and precision (SD) of 2.4.
Pulse oximetry measurements in patients with sickle cell
anemia in this study had a bias of 5.0% and precision (SD)
of 5.3.

The interpretation of pulse oximetry data in pa-
tients with sickle cell anemia is problematic for several
reasons. This instrument is often used as a surrogate for
arterial measurements of PaO₂. Pulse oximetry is reason-
able accuracy for this purpose in patients with normal
oxygen dissociation curves. For example, an oxygen satu-
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saturation of 93% predicts a PaO₂ of 70 mm Hg, and an
oxygen saturation of 90% predicts a PaO₂ of 60 mm Hg.
Clinical judgments are based on the assumption of a nor-
mal P50 of 26.5 mm Hg. Because patients with sickle he-
moglobin can have significant right shift of the oxyhe-
moglobin curves, estimates of PaO₂ based on pulse
oximetry can be grossly inaccurate. In this sample of
children with sickle cell disease evaluated as outpatients, SpO₂
of less than 93% poorly predicted hypoxemia (PaO₂ <70
mm Hg), suggesting that, if used as a marker for ther-
apeutic intervention (ie, supplemental oxygen therapy or
tonsillectomy for suspected obstructive sleep apnea syn-
drome), patients with sickle cell disease may be over-
treated.

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Several investigators have attempted to correlate pulse
oximetry measurements with severity of disease.12,16,17 Rackoff et al12 used pulse oximetry in a group of acutely ill patients with sickle cell disease in the emergency
department to predict the probability of an ACS. Only 5 of 32 patients had an SpO₂ less than 96% and more than 3 points lower than their SpO₂ when well. The pre-
dictive value of a low SpO₂ and developing ACS was 47%.
The predictive value of a low SpO₂ to detect hypoxemia
(PaO₂ <70 mm Hg) was not determined in this study.

Patients may be referred for management of an evolving
crisis and treated with transfusions and supplemental oxygen based on a diagnosis of “hypoxemia” made by pulse
oximetry.

A review of the records of 19 patients with sickle

cell disease who sought medical care in the emergency
department from February 1, 1987, to January 31,
1991, examined the ability of pulse oximetry to predict
PaO₂. There were 93 simultaneous pulse oximetry
(SpO₂) and PaO₂ data. An SpO₂ less than 93% as a pre-
dictor of a PaO₂ less than 80 mm Hg had a sensitivity of
80% and a specificity of 75%. The positive predictive
value was 53%, and the negative predictive value was
91%. These data are consistent with our study of oxim-
etry in patients with sickle cell disease in an outpatient
setting. We suggest, based on our findings, that pulse
oximetry is not a good predictor of hypoxemia in

![Figure 2. Plot of simultaneous oxygen saturation by pulse oximetry (SpO₂) and PaO₂ in individuals with sickle cell disease. The curve depicts the normal oxyhemoglobin relation (the PaO₂ at which the oxygen saturation is 50% = 26.5 mm Hg) defining the expected PaO₂ for a given oxygen saturation. The cross bars depict the ability of pulse oximetry to identify hypoxemia if defined by an SpO₂ less than 93% and a PaO₂ less than 70 mm Hg. The negative predictive value of a pulse oximetry reading greater than 93% was 94% (95% confidence interval, 70%-99%).](https://archpedi.jamanetwork.com/)

**COMMENT**

Pulse oximetry in clinically stable patients with sickle

cell disease evaluated in an outpatient setting had poor

specificity in detecting hypoxemia. Many more patients

would have been considered hypoxic based on pulse

oximetry measurements alone than were actually

hypoxic enough to require intervention. Pulse oximeters

have been validated in healthy, nonsmoking individuals

and have an expected bias of 2% (mean difference

between SpO₂ and SaO₂) and precision (SD) of 2.4.
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patients with sickle cell disease when they are well, and it might not be useful in acute settings if the prevalence of hypoxemia is low.

Treatment of apparent hypoxemia based on pulse oximetry alone (when PaO₂ is actually >70 mm Hg) could be inappropriate, unnecessary, and even dangerous (suppression of erythropoiesis). If a child with sickle cell disease has an SpO₂ less than 93%, an arterial blood gas analysis is needed to validate the result before any therapeutic decisions are made to start supplemental oxygen therapy. Furthermore, there are no data to suggest that the relation between the oxygen saturation and PaO₂ (the P50) is static in an individual with sickle hemoglobin, so further studies of these relations when patients are well and acutely ill should be pursued. In addition, these data suggest that a normal SpO₂ might not require further evaluation. However, because numbers were small, this should be confirmed in larger and more diverse sickle cell populations. In summary, there are multiple sources of potential error in pulse oximetry when used in individuals with sickle hemoglobin, which should be considered when a patient is evaluated for hypoxemia. These data suggest that making treatment decisions based on pulse oximetry data alone in patients with sickle cell disease who are not acutely ill might be inappropriate; correlation of abnormal pulse oximetry values with arterial blood gas determination of PaO₂ and SaO₂ seems to be essential.

Accepted for publication May 10, 2000.

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