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Variability of Pulse Oximetry Measurement Over One Year in Children with Sickle Cell Disease Depends on Initial Oxygen Saturation Measurement

Jonathan E. Mullin¹, Ben Cooper², Sinziana Seicean³, Robert Strunk, MD⁴, Carol Rosen, MD⁵, Susan Redline, MD³, James Kemp, MD⁴, and Michael R. DeBaun, MD⁴

¹Case Western Reserve University School of Medicine, Cleveland, USA

²St. Louis University School of Public Health, St. Louis, USA

³Center for Clinical Investigation, Case Western Reserve University School of Medicine, Cleveland, USA

⁴Department of Pediatrics, Washington University School of Medicine, St. Louis, USA

⁵Department of Pediatrics, Case Western Reserve University School of Medicine, Cleveland, USA

Abstract

A prospective cohort of children with sickle cell disease (SCD) was evaluated to determine the variability of daytime pulse oximetry among three measurements over approximately one year. Fifty-eight participants were evaluated. Asymptomatic children with initial oxygen saturation $\leq 92\%$ had a mean range over one year of 4.6% (2.1% to 7.5%) while clinically stable. In contrast, asymptomatic children whose oxygen saturation was $> 92\%$ had a mean range of 1.9% (0 to 5.5%). These results suggest changes in pulse oximetry measurement of 4.6% may not be clinically significant in otherwise healthy children with SCD with previous pulse oximetry $\leq 92\%$.

Keywords

Sickle Cell Disease; Pulse Oximetry

Introduction

Pulse oximetry assessment of oxygen saturation is commonly used to evaluate individuals with sickle cell disease (SCD). Lower chronic daytime oxygen saturation levels in well children have been associated with recurrent acute chest syndrome (ACS) and pain (1,2). Lower nighttime oxygen saturation levels have been associated with higher rates of pain and CNS events (3,4,5). Despite these findings in some studies, the relationship between oxygen saturation and SCD-related morbidity has been inconsistent (1,2,3,4,5,6,7). This inconsistency may arise, in part, from the variability over time of pulse oximetry readings among individuals with SCD who remain well. Data are limited that describe the longitudinal variability of daytime pulse oximetry readings when the children are not ill. (2)

We examined pulse oximetry measurements from children who participated in the prospective, multi-center, Sleep and Asthma Cohort (SAC) Study. In brief, the SAC study assesses the sleep and respiration of children with SCD, including periodic exams when well. The primary objective of the current analysis was to quantify the variability of daytime resting pulse oximetry readings, measured three times, over approximately 12 months, in children with SCD who were not acutely ill. We also analyzed whether differences in variability in 3 measurements were linked to age, gender or initial oxygen saturation.

Methods

Institutional Review Board approval was obtained at Washington University in St. Louis, and Case Medical Center, Cleveland, Ohio. Pulse oximetry was performed at the time of study enrollment, and repeated at approximately six month intervals during scheduled well visits. Some visits were delayed because the participant did not meet the predefined criteria for a well visit. The criteria for a well visit included absence of any acute medical conditions, including no pain requiring opioids within the previous 48 hours, no hospitalization for acute chest syndrome, or receipt of blood transfusion within 3 months, no hospitalization for a respiratory problem (pneumonia, bronchitis, etc.) within 2 weeks of any study pulse oximetry measurement, and no initiation of chronic blood transfusions, or initiation or discontinuation of hydroxyurea within the study period.

Participants

Participants were ≥ 4 and ≤ 18 years old with previously diagnosed sickle cell disease: HgbSS or HgbS beta thalassemia zero.

Procedure

Oxygen saturation was measured with a finger pulse oximeter (Masimo Radical™). The patient sat calmly and comfortably with minimal or no movement for five minutes while oxygen saturation values were averaged every 2 seconds by the device and a mean percent oxygen saturation for 5 minutes was calculated. A baseline hemoglobin level was defined as the hemoglobin measurement, when otherwise well, drawn closest to the date of Visit 1.

Data Analysis

The mean daytime resting oxygen saturation, over 5 minutes, for Visit 1 was identified as the initial oxygen saturation level. The inter-measurement range for each participant was the greater absolute value of the difference between the initial 5 minute mean and the 5 minute mean of either the second or third visit. Pearson product moment correlations were used to determine the relationship between age and gender and baseline oxygen measurement. Participants were grouped by initial pulse oximetry measurements into those with oxygen saturation $\leq 92\%$ and those with oxygen saturation $>92\%$ at the initial measurement. Ninety-two percent was chosen a priori because this value is often used as the cut-off point when assessing disease severity in patients with acute respiratory illnesses. (8,9) The Wilcoxon rank sum test was used to compare the oxygen saturation ranges of the $\leq 92\%$ and $>92\%$ groups. Pearson correlations were used to determine the correlation between hemoglobin levels, hydroxyurea use, oxygen saturation and range of oxygen saturation.

Results

Seventy-six SAC participants had three pulse oximetry measurements at approximately six months intervals. Fifty-eight participants met all the inclusion criteria. Mean interval between first and last pulse oximetry measurement was 467 days (range: 314 to 801). For

scheduling reasons, three patients had their third pulse oximetry measurement less than one year after the first, at 314, 350 and 364 days. These patients were included in the analysis.

For all 58 participants, mean initial oxygen saturation was 95.6% ($\pm 3.3\%$ SD). Using the greater absolute value of the difference between the initial 5 minute mean and the 5 minute mean of either the second or third visit as the inter-measurement range, the mean inter-measurement range was 2.4% (range= 0 to 7.5). Neither age ($p=0.21$) nor gender ($p=0.47$) were associated with initial oxygen saturation. Inter-measurement range, the range between three measurements for an individual, was negatively correlated with baseline oxygen saturation level ($r=-0.67$, $p<0.001$). Participants with a mean oxygen saturation $\leq 92\%$ ($n=10$) had a mean inter-measurement range of 4.6% (range: 2.1 to 7.5); participants with a mean saturation $>92\%$ ($n=48$) had a mean inter-measurement range of 1.9% (range: 0 to 5.5), Figure. The difference between these two groups was statistically significant (<0.001). Of the 10 participants with initial pulse oximetry measurements $\leq 92\%$, 5 had pulse oximetry measurements $>92\%$ at both subsequent visits, 4 had one pulse oximetry measurement $>92\%$ and one pulse oximetry measurement $\leq 92\%$, and 1 had pulse oximetry measurements $\leq 92\%$ at both subsequent visits.

A total of 12% (7 of 58) participants were on hydroxyurea for the course of the study. These 7 participants had an initial oxygen saturation of 98.4% and a mean inter-measurement range of 1.85, compared to an initial oxygen saturation of 95.3% ($p=0.018$) and mean inter-measurement range of 2.46 ($p=0.387$) for those participants not on hydroxyurea. There was no difference in baseline hemoglobin level for those patients on or not on hydroxyurea, 7.97 g/dL and 8.19 g/dL, respectively. ($p=0.327$)

A total of 97% (56 of 58) participants had a baseline hemoglobin level, mean and median number of days between baseline hemoglobin measurement and initial pulse oximetry measurement were 87.2 days and 50 days, respectively. Baseline hemoglobin level was positively correlated with initial oxygen saturation ($R= 0.374$ $p=0.005$).

Discussion

Understanding the range of pulse oximetry measurements obtained when free from acute illness is essential for clinical management of children with SCD. We have shown that the range of pulse oximetry measurements is dependent on the value when the participant was first evaluated. For the 10 participants with an initial mean oxygen saturation level $\leq 92\%$, a larger range existed, 4.6 percentage points, as compared to the 58 participants with an initial oxygen saturation $>92\%$, 1.9 percentage points.

The wider range of pulse oximetry measurements when the initial oxygen saturation was lower might be explained by the individual saturation's proximity to the point of inflection of the sigmoid-shaped oxygen dissociation curve. At this position, small changes in the partial pressure of oxygen in blood may cause greater changes in the measured oxygen saturation level. These findings are relevant because approximately 15% of children with SCD have a baseline oxygen saturation near the expected point of inflection (85% to 92%). (7)

At least five explanations exist for the increased variability of pulse oximetry measurements over one year in children with SCD whose initial pulse oximetry is $\leq 92\%$. First, as noted above, participants with oxygen saturation near the point of inflection of the oxygen dissociation curve would be expected to have small changes in oxygen tension that result in larger changes in oxygen saturation, as compared to participants with higher oxygen saturation. Second, the children with initial pulse oximetry $\leq 92\%$ may have been ill at the initial visit in ways that were missed by our exclusion criteria. In this case, the increased

variability may be a result of these patients recovering from illness, with improving pulse oximetry measurements. Third, the phenomenon of regression to the mean could be responsible for patients with low initial measurements having higher subsequent measurements that are closer to the group mean. (10) Fourth, as reported by others (6), hemoglobin measurements had a positive association with oxygen saturation at the initial visit. Hemoglobin measurements were not taken at subsequent study visits within 12 months of the initial visit, and thus we could not determine if the variation in hemoglobin levels contributed to the variability of oxygen saturation measurements. Lastly, a combination of all four factors may contribute to this variability. Our study design does not allow us to distinguish between these possibilities.

Based on our results, we suggest that low pulse oximetry measurements obtained from children with SCD at a routine clinic visit should not necessarily prompt further laboratory evaluation, when the patient is asymptomatic and has a history of low pulse oximetry measurements. Children without symptoms, but with low pulse oximetry measurements require a reassessment of history and physical examination, but do not necessarily require a full evaluation with an arterial blood gas, chest radiography or other diagnostic tests. These clinical decisions are best made on case-by-case bases. Our results suggest that some low pulse oximetry measurements in asymptomatic children with SCD may not represent a change in clinical status over the course of one year.

In summary, in children with SCD, interpretation of oxygen saturation when well requires a thorough history, physical examination and knowledge of the variability of pulse oximetry measurements.

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Figure 1.

Inter-measurement range of oxygen saturation of three measurements when well, plotted as a function of baseline oxygen saturation in children (n=58) with hemoglobin SS disease or hemoglobin S beta thalassemia zero. ($r=.67$, $p<0.001$)