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Accuracy of Noninvasive and Continuous Hemoglobin Measurement by Pulse Co-Oximetry During Preoperative Phlebotomy

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Abstract

Background: In recent years, the continuous noninvasive hemoglobin measurement has been offered by devices using advanced pulse oximetry technology. Accuracy has been established in healthy adults as well as in surgical and intensive care unit patients but not in the setting of acute hemorrhage. In this study, we evaluated the accuracy of such a device in the clinical setting of preoperative phlebotomy thereby mimicking a scenario of acute blood loss. **Methods:** This prospective study included patients undergoing surgical repair of congenital heart disease (CHD) for whom preoperative phlebotomy was planned. Blood was removed after the induction of anesthesia and prior to the start of the surgical procedure. Replacement with crystalloid was guided by hemodynamic variables and cerebral oxygenation measured by near-infrared spectroscopy. Hemoglobin was measured by bedside whole blood analysis (total hemoglobin [tHb]) before and after phlebotomy, and concurrent measurements from the pulse co-oximeter (noninvasive, continuous, or spot-check testing of total hemoglobin [SpHb]) were recorded. **Results:** The study cohort included 45 patients ranging in age from 3 months to 50 years. Preoperative phlebotomy removed an average of 9.2 mL/kg of blood that was replaced with an average of 7.2 mL/kg of crystalloid. The pre- and postphlebotomy tHb values were 13.0 $\pm$ 1.9 and 12.4 $\pm$ 1.8 g/dL, respectively. The absolute difference between the tHb and SpHb (ΔHb) was 1.2 $\pm$ 0.1 g/dL. Bland-Altman analysis revealed a bias of 0.1 g/dL, a precision of 1.5 g/dL, and 95% limits of agreement of $-$2.8 to 3.1 g/dL. In 52.2% of the sample sets, the SpHb was within 1 g/dL of the actual hemoglobin value (tHb), and in 80% of the sample sets, the SpHb was within 2 g/dL. No variation in the accuracy of the deviation was noted based on the patient's age, weight, or type of CHD (cyanotic versus acyanotic). **Conclusion:** The current study demonstrates that the accuracy of continuous, noninvasive hemoglobin measurement was not affected by acute blood loss simulated by preoperative phlebotomy. Although the device provided a clinically acceptable correlation with the actual hemoglobin value and offers the value of a continuous trend monitor, given the precision of the device, it does not appear that actual transfusion decisions can be based on the device alone.

Keywords

Non invasive hemoglobin monitoring, Acute normovolemic hemodilution, Monitoring and pediatric cardiac surgery

Introduction

Recent advances in pulse oximetry technology have resulted in the development of noninvasive pulse oximeters that provide a continuous readout of not only the oxygen saturation but also the hemoglobin value.[1-5] The accuracy of these monitors has been validated in various clinical scenarios including the intensive care unit (ICU) and the operating room. To date, there are limited data regarding the performance of such devices during periods of acute blood loss. At our institution, as a means of avoiding allogeneic blood products, we routinely perform preoperative phlebotomy in our cardiac surgical population.[6] This practice involves the removal of autologous blood in the operating room after the induction of anesthesia.

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In many centers, the technique of acute normovolemic hemodilution is performed whereby a quantity of the patient's whole blood is removed prior to surgical incision replaced by a 3:1 ratio of crystalloid or 1:1 ratio of colloid to maintain euvolemia.[7] However, the replacement fluid and hemodilution may be problematic in patients that are subsequently placed on cardiopulmonary bypass (CPB), as the secondary hemodilution from the crystalloid prime of the CPB circuit will further dilute the blood and result in a hemoglobin that is too low for CPB.[8,9] Therefore, in our practice, the autologous blood is removed with the majority of patients receiving less than 1 mL/kg of crystalloid in fluid replacement for each 1 mL/kg of blood that is removed.[10] As such, the clinical scenario may resemble what is seen during acute blood loss. Given this opportunity, we prospectively studied the efficacy and accuracy of a commercially available pulse oximeter that provides a continuous readout of not only the oxygen saturation but also the hemoglobin value (Radical 7; Masimo Corporation, Irvine, California). Furthermore, information is provided regarding the accuracy of this novel device in patients with cyanotic congenital heart disease (CHD).

Methods

This study was approved by the institutional review board of Nationwide Children's Hospital, and the need for informed consent was waived. Data were collected prospectively from patients undergoing operative repair of CHD for whom presurgical phlebotomy was planned to minimize the need for allogenic blood products. Following the induction of general anesthesia with standard monitoring according to the standards of the American Society of Anesthesiologists, the Masimo pulse co-oximeter (Radical 7, software 7.6.2.1; Masimo Corporation) was applied to the patient's finger using a disposable probe (adult & pediatric Resposable Rev E R2-20 & R2-25 and Adhesive Rev E R1-20L). The manufacturer's reported accuracy of this device is ± 1 g/dL hemoglobin. When a radial or ulnar arterial cannula was placed, the pulse oximeter probe was placed on the opposite hand. The probe was placed on the ring or index finger. Body temperature was continuously monitored and maintained during data collection at 36°C to 37°C by adjusting the temperature of the environment. Total hemoglobin (tHb) was measured at the bedside from whole blood optical analysis (AVOXimeter, ICTMed; Optimedical, Edison, New Jersey), and the concurrent readings were noted from the Masimo pulse co-oximeter (noninvasive, continuous, or spot-check testing of total hemoglobin [SpHb]) prior to the start of phlebotomy and then at the completion of phlebotomy. As point-of-care (POC) testing for hemoglobin and blood gas analysis is the standard of care in most operating rooms, we chose to use this method of hemoglobin determination for comparison to the pulse oximeter values. The manufacturer's stated accuracy for hemoglobin measurement of the device is 0.45 g/dL at hemoglobin values greater than 10g/dL and 0.35 g/dL at values less than 10 g/dL (AVOXimeter 1000E4000 Sell Sheet, ICTMed; Optimedical).

Table 1. Surgical Procedures Performed in the Study Cohort.

Surgical Procedure	Number of Patients
Aortic root or valve replacement or repair	9
Pulmonary valve replacement	9
Atrial or ventricular septal defect repair	9
Subaortic stenosis or membrane repair	4
Comprehensive stage II procedure	3
Fontan operation	3
Anomalous pulmonary venous return repair	3
Transposition of the great vessels	2
Tricuspid valve replacement/repair	2
Tetralogy of Fallot	2
Left superior vena cava ligation	1
Glenn procedure	1
PDA repair	1
Mitral valve repair	1

Abbreviation: PDA, patent ductus arteriosus.

Phlebotomy was performed over a 5- to 10-minute period through a central venous catheter or an arterial cannula. The volume of blood removed was calculated based on the patient's weight, starting hematocrit, and a target hematocrit after the initiation of CPB of 24% to 28%. Hemodynamic values including mean arterial pressure and heart rate as well as cerebral oxygenation measured by near-infrared spectroscopy were monitored during phlebotomy. A greater than 20% change from the baseline in these parameters was remedied by some combination of volume replacement with crystalloid, administration of phenylephrine, or temporary cessation of phlebotomy.

Statistical analysis included a nonpaired *t* test and a Bland-Altman plot to compare the hemoglobin values from the pulse co-oximeter (SpHb) with the values from the POC hemoglobin monitor (tHb). In calculating the differences between the 2 devices, the absolute difference was first used to avoid biasing the data by including both negative and positive numbers. During the Bland-Altman analysis, per convention, both positive and negative numbers were used in the calculation of the bias. A contingency table with the Fisher exact test was used to determine whether any patient characteristics such as age, weight, or type of CHD (cyanotic vs acyanotic) were associated with a greater incidence of disparity between the SpHb and the tHb. The data are listed as the mean $\pm$ standard deviation (SD) with $P < .05$ considered significant.

Results

The study cohort included 50 patients; however, 5 patients were excluded for protocol violations including a missing SpHb value at one point in four and a missing tHb reading in one. This left a cohort of 45 patients ranging in age from 3 months to 50 years (13.1 $\pm$ 12.9 years; median 10 years) and in weight from 4.7 to 131 kg (41.5 $\pm$ 33.1; median 33 kg). The spectrum of CHD repair operations is represented in Table 1. The starting hemoglobin value from the POC monitor (tHb) was 13.0 $\pm$ 1.9 g/dL (P = nonsignificant [NS]). There was a

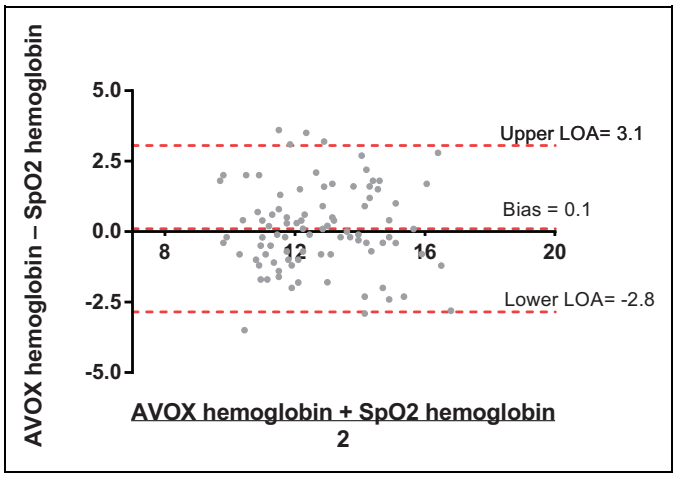

Figure 1. Bland-Altman comparison plotted as the difference between the laboratory (AVOX) and the pulse co-oximeter (SpHb) hemoglobin values on the y axis versus the average of the 2 values on the x axis. The bias and level of agreement (LOA) are shown in horizontal lines. SpHb indicates noninvasive, continuous, or spot-check testing of total hemoglobin.

Table 2. Number of Patients With Specific Differences Between Laboratory (tHb) and Pulse Co-oximeter Hemoglobin Values (SpHb).

Difference Between the Laboratory and Pulse Co-Oximeter Hemoglobin Value, g/dL	Number of Values Prior to Phlebotomy	Number of Values Following Phlebotomy	Total Number of Values
≤1	22 (48.9%)	25 (55.6%)	47 (52.2%)
>1 and <2	17 (37.8%)	8 (17.8%)	25 (27.8%)
≥2 and <3	5 (11.1%)	8 (17.8%)	13 (14.4%)
≥3	1 (2.2%)	4 (8.9%)	5 (5.6%)
Total	45	45	90

Abbreviations: SpHb, noninvasive, continuous, or spot-check testing of total hemoglobin; tHb, total hemoglobin.

total of 9.2 ± 3.1 mL/kg of blood removed during preoperative phlebotomy, with the administration of 7.2 ± 6.5 mL/kg of crystalloid. The postphlebotomy tHb value was 12.4 ± 1.8 g/dL.

The SpHb and tHb were obtained at the start and completion of phlebotomy in 45 patients providing 90 sample sets for comparison. Using the absolute values (no plus or minus values), the tHb − SpHb difference (ΔHb) was 1.2 ± 0.9 g/dL for the 90 sample sets. There was no difference in the ΔHb between the 45 sample sets obtained before phlebotomy and those obtained after phlebotomy (1.2 ± 0.8 g/dL vs 1.2 ± 1.0 g/dL, P = NS). When considering the 90 sample sets, Bland-Altman analysis revealed a bias of 0.1 g/dL, a precision of 1.5 g/dL, and 95% limits of agreement of −2.8 to 3.1 g/dL (Figure 1). The SpHb value was within 1 g/dL of the tHb in 47 (52.2%) of the 90 sample sets and within 2 g/dL in 72 (80%) of the 90 sample sets (Table 2). The largest disparity in values, occurring at one point following phlebotomy, was a SpHb that was 3.6 g/dL higher than tHb. When the SpHb deviated from tHb, the deviation was just as likely to be in a positive as negative direction (48% vs 52%).

There were 15 data points from 9 patients, in which the signal quality (SIQ) was noted as low (<50%). At 4 of these 15 points, the ΔHb was ≥2 g/dL, and at 2 points it was ≥3g/dL. If these data with low SIQ are excluded, the ΔHb was ≤2 g/dL in 62 (83%) of the 75 sample sets, which is no different from the complete set of 90 data points. Likewise, no difference was noted in the ΔHb (1.1 ± 0.9 vs 1.2 ± 0.9, P = NS), when the SIQ was less than 50%.

When comparing groups of patients based on the frequency of ΔHb ≤ 1 g/dL versus ≥2 g/dL, there was no statistically significant difference in the age, weight, starting hemoglobin, volume of blood removed, fluid administered, or type of CHD (cyanotic vs acyanotic; Table 3). When comparing patients ≤ 4 years of age to those older than 4 years of age, there was a significant difference in the volume of blood removed (11.1 ± 2.9 vs 8.1 ± 2.6 mL/kg, $P = .0008$) and fluid administered (11.1 ± 7.5 vs 4.87 ± 4.5 mL/kg, $P = .0009$). However, there was no statistically significant difference in the frequency or degree of agreement between the tHb and the SpHb values. This was also true when patients were grouped as ≤1 versus >1 year of age. Fourteen patients had a cyanotic heart defect; and although they were generally younger (7.7 vs 15.6 years), there was no significant association between ΔHb and type of CHD (Table 4). Linear regression analysis of hemoglobin measurements revealed an r value of .71 and r^2 value of .51 for prephlebotomy readings. For postphlebotomy readings, the r and r^2 values were .64 and .41, respectively. When considering all measurements, the r value was .68, and r^2 was .46 (P = NS vs prephlebotomy readings).

Discussion

In recent years, there has been an increased recognition of the need for as well as the acceptance of POC measurement of several laboratory parameters. During periods of rapid blood loss and replacement such as patients with trauma or during intraoperative hemorrhage, the availability of an accurate means of continuously and noninvasively monitoring hemoglobin may be useful. With advances in pulse oximetry technology, there are commercially available devices that provide a continuous readout of the hemoglobin value in addition to the oxygen saturation. These devices have been evaluated in both the ICU and the operating room settings.[2-5] Although the latter provides an arena where acute blood loss may occur, to our knowledge, no study has focused on the accuracy of these devices during the period of acute blood loss. Our clinical practice in the cardiac operating rooms provides a scenario where 8 to 10 mL/kg of blood is rapidly removed over 5 to 10 minutes prior to the start of the surgical procedure. This autologous blood is then reinfused following CPB to reduce the need for postoperative allogeneic blood products. The rapidity of the blood removal and the limited volume replacement administered are demonstrated by the minimal change in the actual hemoglobin before and immediately following

Table 3. Comparative Demographics of Patients With Differences ≤1 versus ≥2 g/dL.

Laboratory and Pulse Co-Oximeter Hemoglobin Difference, g/dL	Number of Values	Age, years	Weight, kg	Starting Hemoglobin, g/dL	Volume of Blood Removed, mL/kg	Crystalloid Administered, mL/kg	Postphlebotomy Hemoglobin, g/dL
≤1	18	12 ± 9.4	38.9 ± 25.3	12.9 ± 1.8	9.4 ± 2.6	7.7 ± 8.7	12.3 ± 1.6
≥2	15	12.7 ± 15.1	36.6 ± 32.3	13.4 ± 2.6	9.9 ± 3.2	7.1 ± 4.4	12.6 ± 2.5

Table 4. Pulse Co-Oximeter Hemoglobin Accuracy in Varying Age Groups and Type of Cardiac Defect.[a]

	Age, years				Cyanotic Heart Defect (n = 14)	Noncyanotic Heart Defect (n = 31)
	≤1 (n = 11)	>1 (n = 34)	≤4 (n = 17)	>4 (n = 28)		
ΔHb prephlebotomy	1.54 ± 0.9	1.1 ± 0.7	1.3 ± 0.8	1.1 ± 0.8	1.1 ± 0.9	1.2 ± 0.7
ΔHb postphlebotomy	1.4 ± 1.2	1.1 ± 1.0	1.4 ± 1.2	1.0 ± 0.9	0.9 ± 0.8	1.3 ± 1.1
ΔHb overall	1.4 ± 1.1	1.1 ± 0.9	1.4 ± 1.0	1.1 ± 0.9	1.0 ± 0.9	1.3 ± 0.9
ΔHb > 2 g/dL	7 of 22	11 of 68	9 of 34	9 of 56	5 of 28	13 of 62

Abbreviation: SD, standard deviation.

[a] The ΔHb hemoglobin (difference between the laboratory and the pulse oximeter value) is listed as the mean ± SD. In calculating the difference, absolute differences were used so that if the difference was above or below the actual value, a positive difference was used to avoid biasing the mean.

phlebotomy in our cohort of 45 patients (13.0 ± 1.9 vs 12.4 ± 1.8 g/dL). Furthermore, during periods of rapid blood loss, one would not expect a rapid change in the hemoglobin value until fluid shifts correct for the associated hypovolemia.

In this setting, we found that the commercially available pulse oximeter used in the current study provided a clinically relevant estimation of the actual hemoglobin value, with more than 80% of the values being within 2 g/dL of the actual value. However, given that only 50% of the values were within 1 g/dL, it is unlikely that decisions regarding the choice to transfuse allogeneic blood can be solely based on the device. We noted no alteration in the accuracy of the device when comparing values obtained prior to and immediately following phlebotomy. This accuracy would be mandatory when such devices are used in the trauma setting or intraoperatively when acute blood losses may occur. Additionally, when considering its use in patients with cyanotic CHD, we saw no deviation in the accuracy of the device in this subset of the study cohort.

Previous studies have revealed conflicting results on the accuracy of the pulse co-oximetry for hemoglobin determination. A prospective observational study by Frasca et al compared the Masimo Radical-7 pulse co-oximeter hemoglobin value to laboratory reference measurements as well as to other POC devices.[2] A total of 471 blood samples were obtained from 62 patients in a surgical ICU. They noted a correlation coefficient of 0.79 with a bias and limits of agreement of 0.0 ± 1 g/dL. They also noted accurate performance of the device when the perfusion index was lower than 0.5 with a bias of 0.4 as well as during the administration of norepinephrine (bias = −0.1). The investigators concluded that noninvasive hemoglobin measurement with the pulse co-oximeter had absolute and trending accuracy similar to widely used laboratory methods of hemoglobin measurement.

Macknet et al compared the hemoglobin values measured by pulse co-oximetry to laboratory reference values.[3] Each patient had approximately 500 mL of blood removed, which was replaced with up to 30 mL/kg or until a 30% reduction in the hemoglobin value was achieved. A total of 165 laboratory hemoglobin measurements were paired to 335 pulse oximeter values; and in 90% of cases, the difference between the 2 measurements was ≤1.5 g/dL. Overall, the difference (mean ± SD) was −0.15 ± 1.0 g/dL. Similar results were additionally noted in a study using 186 data pairs from 29 patients during complex spinal surgery, although the authors excluded 56 data pairs where the SIQ was low.[4] Eighty-eight percent of the SpHb values were within 1.5 g/dL of the laboratory reference value, with a bias and a precision of −0.1 g/dL and 1.0 g/dL, respectively.

By contrast, Nguyen and colleagues reported a poor correlation between hemoglobin values obtained by the pulse co-oximeter with those obtained from an automated hematology analyzer.[5] A total of 103 paired data points from 41 adult patients in a cardiac ICU were reviewed. In 27 patients, the newer version of the pulse oximeter software (7.3.1.1) was used. With the newer version of the software, the bias was −1.7 g/dL, with 95% confidence intervals of −2.3 and −1.1 g/dL. The bias was not significantly different for the 14 patients in whom the older software version (7.3.0.1) was used. The coefficient of determination (R^2) was .11 and .27 with the older and newer software, respectively. The authors concluded that their study demonstrated a poor correlation between hemoglobin measured noninvasively by multiwavelength pulse oximetry and a laboratory hemoglobin analyzer. They also noted that the difference was greater when the perfusion index was low. However, the investigators used a clip-on sensor indicated for spot checking rather than

continuous measurements. This may have contributed to the difference in their results.

In an emergency department setting, Gayat et al compared hemoglobin measurements from the multiwavelength pulse co-oximeter and laboratory devices in 276 patients and concluded that the pulse co-oximeter measurements were too unreliable for the device to be recommended.[11] They reported a bias of 1.8 g/dL with upper and lower limits of agreement of −3.3 and 6.9 g/dL. Thirteen percent of the data pairs were in disagreement such that one value was above and the other below 9.0 g/dL, which the authors suggested may lead to erroneous decision making regarding transfusion. However, the manufacturer of the pulse co-oximeter used for the study noted several methodological issues with the study including that the device was not used according to the manufacturer's directions, and an adhesive probe indicated for continuous measurement was used instead of a reusable probe indicated for spot check measurements.[12]

There are certain limitations to our current study, which may have impacted the results. Only a single postphlebotomy value was obtained, and therefore, we cannot comment on the utility or accuracy of the device following cannulation and institution of CPB. The device used to provide the reference hemoglobin (tHb) is a portable, spectrophotometric co-oximeter, which may vary from the gold standard for hemoglobin measurement, the cyanomethemoglobin assay. Additionally, the SpHb accuracy has not been validated for conditions of low oxygen saturation or low perfusion. Although we noted no such variation in our study, the manufacturer's directions for use indicate that low arterial oxygen saturation levels or a low SIQ (less than 50%) may cause inaccurate SpHb readings. Therefore, the performance of pulse co-oximetry for hemoglobin measurement may be different during acute blood loss in other patient populations.

Despite these concerns, we noted a clinically acceptable correlation with the laboratory hemoglobin values for trend monitoring. However, it has been emphasized that in order to be a truly effective monitor, such devices should be accurate enough so that a transfusion decision can be based on their parameters.[10] To accomplish such practices, the device would likely need to be accurate within 1 g/dL, especially in the critical range where transfusion would be considered (6-8 g/dL). In the current study, we had no patients with a hemoglobin value in this range, so we cannot definitively comment on such performance. However, given that only 50% of the values in our current study were within 1 g/dL, it is unlikely that the current technology would provide an accuracy adequate for decisions regarding the need for transfusion. However, we found that the device was accurate enough to allow it to be used as a clinically useful trend monitor. It functioned effectively even during the period of rapid blood loss (approximately 10 mL/kg over 5-15 minutes).

Authors' Note

The pulse oximeter and disposable probes used in the current study were provided free of charge by the manufacturer.

Declaration of Conflicting Interests

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