A Comparison of Three Methods of Hemoglobin Monitoring in Patients Undergoing Spine Surgery

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BACKGROUND: Hemoglobin values (Hb) can facilitate decisions regarding perioperative transfusion management. Currently, Hb can be determined invasively by analyzing blood via laboratory Co–Oximetry (tHb) or by point-of-care HemoCue (HCue). Recently, a new noninvasive, continuous spectrophotometric sensor (Masimo SpHb) was introduced into clinical practice. We compared the accuracy of the SpHb and HCue with tHb.

METHODS: Twenty patients, ages 40 to 80 years, were studied. They received general anesthesia and underwent spine surgery in the prone position. All blood samples were obtained from a radial artery catheter. SpHb, tHb, and HCue were determined immediately after induction of anesthesia, but before the start of surgery and approximately every hour thereafter. Primary outcomes were defined on the basis of the following differences between measures: SpHb – tHb or HCue – tHb. All patients had 3 to 5 observations taken on each measure. Differences and absolute differences were analyzed by several techniques to assess accuracy. We also investigated the relationship between observed differences and the following variables: tHb level, duration of surgery, age, weight, and perfusion index.

RESULTS: Data consisted of 78 measurements of SpHb, tHb, and HCue made on the 20 patients. Absolute differences between SpHb and tHb were <1.5 g/dL for 61% of observations, between 1.6 to 2.0 g/dL for 16% and >2.0 g/dL for 22% of the observations. Observed differences displayed significant decreases with time and higher perfusion index values. No systematic relationships were observed with age or weight. Except for 1 value, all of the HCue values were <1.0 g/dL of tHb.

CONCLUSIONS: Although HCue was consistently accurate, our data confirm that SpHb often correlated well with tHb values. Yet our study indicates that SpHb may not be as accurate as clinically necessary in some patients. Improved refinement of continuous, noninvasive technology, such as SpHb, could address important clinical requirements. (Anesth Analg 2011;112:858–63)

The specific “transfusion trigger” that is the threshold for administering packed red blood cells or whole blood has been debated for years.1–3 Many clinical variables, especially assessment of intravascular volume, hemoglobin (Hb) levels, and their association with each other, are used to determine the amount, timing, and type of fluid to be administered.4 In a hypovolemic patient, an Hb level of <10 g/dL may indicate the need for a blood transfusion, whereas for all patients a level of <7.0 g/dL generally indicates the need for transfusion. Currently, the clinician must make 2 decisions: when to measure the Hb level and, on the basis of the results, when to transfuse blood. Sending a sample of the patient’s blood to the laboratory allows Hb to be measured by a Co–Oximeter device (tHb). Alternatively, a sample of the patient’s blood can be analyzed for Hb using a point-of-care-HemoCue (HCue) device5 in the operating room or at the bedside.

Until recently, these intermittent and invasive monitoring methods were the only ones available to assess Hb levels and required making a decision about the timing of sampling on the basis of clinical conditions.4 A new device is now available that allows Hb concentrations to be continuously and noninvasively monitored using the Masimo Radical 7 Pulse Co–Oximeter with SpHb™ sensors, and software for the study.

We propose that SpHb has sufficient accuracy to minimize the need for invasive Hb monitoring, such as with tHb or HCue. To test this hypothesis, we compared Hb levels from the SpHb with those invasively derived and analyzed them with standard laboratory Co–Oximeter (tHb) and HCue5 methods. The study was performed in patients undergoing general anesthesia and spine surgery in the prone position.

There are several variables that could influence the difference between the SpHb and tHb. We examined some of these variables including tHb itself, duration of surgery, patient weight, and age. In addition, peripheral perfusion at the site of the measurement of SpHb may influence the
detected of Hb levels. To assess this variable, we correlated SpHb – tHb differences with perfusion index (PI), an indirect measure of the perfusion of the finger using plethysmography.7

**METHODS**

**Patients and Data Collection**

After approval from the University of California, San Francisco, Human Research Protection Program, 20 patients, 40 to 80 years of age, were studied. All were undergoing spine surgery in the prone position under general anesthesia and had provided written informed consent preoperatively. They were between 50 and 120 kg in weight. All patients had radial artery catheters inserted as part of their routine anesthetic care.

Hb levels were continuously monitored with the Masimo Radical 7 Pulse Oximeter with SpHb™ and Rainbow Adult Adhesive sensors, version Rev E (Masimo Corporation, Irvine, California) (SpHb). The sensors were covered with an optical shield (provided by Masimo) to prevent optical interference. In addition, Hb levels were determined with a blood sample analyzed by Co-Oximetry (tHb, Beckman–Coulter) in the University of California, San Francisco Clinical Laboratories, and HemoCue™ (HCue, HemoCue AB, 262 23, Angelholm, Sweden) by anesthesia providers in the operating room. The anesthesia providers completed quality assurance training before using the HCue monitor.

All patients had 3 to 5 sets of Hb data collected. Each set is based on simultaneous recording of both an SpHb value with an arterial blood sample drawn for tHb and HCue determination. An initial set was collected before surgical incision, but after the patient was anesthetized and placed in the prone position for the surgery. After the beginning of surgery, blood samples were taken on approximately an hourly basis. The type and amount of intravascular fluids given by the anesthesia team were recorded, including crystalloids, colloids, and all blood products.

Hb analysis for the purpose of our study ended after completion of the surgical procedure. The data from the SpHb (RevE, the commercially available version of the software at the study initiation), tHb, and HCue were recorded manually. Subsequently, the SpHb data were also analyzed by RevF software (another computer program not yet commercially available).

**Statistical Analysis**

Accuracy was assessed by comparison of SpHb with tHb values measured at the same time point. The primary outcome for analysis was the difference between these measures, defined as SpHb minus tHb (SpHb – tHb), and calculated after each measurement occasion for each patient. Initial analyses summarized the distributions of observed differences using means, medians, and ranges. Following the approach recommended by Bland and Altman,8 we summarize bias as the mean difference between measures, and the 95% limits of agreement by the interval defined by the observed bias plus/minus twice the observed SD of the observed differences. Because of possible within-individual correlation between successive measurements, standard deviations were estimated using mixed effect linear regression models for linked replicate measurements, including patient and method level effects.9 The resulting limits of agreement have a prediction interval interpretation, and are generally somewhat wider than the standard Bland–Altman limits. Alternative limits computed with standard deviations on the basis of robust variance estimates10 were comparable, indicating that results are not unduly influenced by the assumptions underlying the linear modeling approach.

These outcome measures were subdivided into 5 groups (on the basis of absolute differences between SpHb and tHb) of <0.5, 0.5 to 1.0, 1.1 to 1.5, 1.6 to 2.0, and >2.0 g/dL, and the group membership proportions summarized with 95% confidence intervals (CIs). Standard errors for confidence limits controlled for repeated outcome observations from each participant by using generalized estimating equation (GEE) methods.10 The distribution of observations into groups was compared between initial measurements taken before surgical incision and those taken after surgical incision with a multinomial logistic regression model, with the outcome based on a categorical variable defining the 5 groups, and with a binary indicator of whether each measurement was taken pre- or postsurgical incision as the predictor. This analysis also controlled for repeated outcome observations using the GEE approach.

We also used graphical techniques to help visualize the observed differences between SpHb and tHb measurement, taking the latter as the true measure of Hb level. Similar to the “error analysis grid” approach described by Clarke et al.,11 the possible values for each pair of measurements on a scatterplot were divided into zones corresponding to differing degrees of absolute percentage difference between SpHb and tHb [defined as 100 × (SpHb – tHb)/tHb].

Additional analyses were conducted to investigate the effect of several variables on the observed SpHb – tHb differences, including measured tHb level, time elapsed (in minutes) after the start of the procedure, patient body weight, and age. These analyses included scatterplot summaries of the relationship between observed differences and these variables, including smoothed lines estimated using locally weighted smoothing12 to illustrate possible trends. Linearity of observed trends was assessed by the slope of a linear regression line fitted to the observed points, with variability summarized by the associated 95% confidence interval (computed using the GEE approach).10 Significance at the 5% level was concluded if the confidence intervals excluded a slope of zero. We also investigated the possible presence of a nonlinear trend by examining the significance of a quadratic term added to the linear models just described.

The function of the SpHb sensor is dependent on adequate bloodflow to the finger as indirectly reflected by the PI. The PI is a calculated value that is displayed with the SpHb. Accordingly, we also investigated the relationship between SpHb – tHb values with the PI using the approach described above. Because obtaining SpHb values with a PI <1.4 is not recommended by the manufacturer, we repeated the above analyses for PI divided into 2 groups and compared those with values <1.4 and those ≥1.4.
RESULTS

One representative actual record of our continuous measurements of SpHb and intermittent measurement of tHb is shown in Figure 1. A total of 78 paired Hb samples were collected and analyzed from 20 patients. Each individual pair contained 1 value from the SpHb monitor display and 1 value from a laboratory determination of tHb. In addition, each patient had a HCue determination of Hb performed simultaneously. Our primary outcome variable was the difference between SpHb and tHb. We also considered the absolute difference as an overall measure of error in measurement by SpHb.

To display the overall pattern of results, we categorized the 78 paired absolute differences into 1 of 5 groups on the basis of the magnitude of the differences. The results from both the RevE and RevF (in parentheses) programs are displayed for each of these groups in Table 1. Results from initial measurements (obtained after induction of anesthesia and positioning but before the start of surgery) are displayed separately from those measurements during surgery. Table 1 shows that the patterns of observed absolute differences are similar in initial measurements to those taken during surgery. Overall, 48 (61%) (95% CI: 43%, 77%) SpHb values corresponded with tHb values by $\leq 1.5$ g/dL. The corresponding percentage of SpHb values differing from tHb values by $>2.0$ g/dL was 17 (22%) (95% CI: 12%, 37%). One patient had tHb high at one point and then lower than SpHb at another point. In all other patients, the SpHb remained either higher or lower than tHb during the surgery. Except for 1 value, all of the HCue values were $<1.0$ g/dL different from the tHb values (Table 2).

The error analysis grid shown in Figure 2 complements the results in Table 1. Basically, 24% of the SpHb measurements were within 5% of corresponding tHb measurements, 55% deviated from tHb by between 6% and 20%, and 21% deviated from tHb by $>20%$.

Table 1. Groups Based on Magnitude of Differences Between Noninvasive (SpHb) and Laboratory Co-Oximeter (tHb) Hemoglobin Concentration (g/dL)

<table>
<thead>
<tr>
<th>Group</th>
<th>&lt;0.5 g/dL</th>
<th>0.5–1.0 g/dL</th>
<th>1.1–1.5 g/dL</th>
<th>1.6–2.0 g/dL</th>
<th>$&gt;2.0$ g/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial (SpHb – tHb) a</td>
<td>4 (4)</td>
<td>3 (6)</td>
<td>4 (5)</td>
<td>4 (3)</td>
<td>5 (2)</td>
</tr>
<tr>
<td>All other (SpHb – tHb) a</td>
<td>15 (6)</td>
<td>8 (21)</td>
<td>14 (12)</td>
<td>9 (11)</td>
<td>12 (8)</td>
</tr>
<tr>
<td>Total</td>
<td>19 (10)</td>
<td>11 (27)</td>
<td>18 (17)</td>
<td>13 (14)</td>
<td>17 (10)</td>
</tr>
</tbody>
</table>

a The RevE software was the computer program generating the SpHb results that were manually recorded during the study. The RevF software (in parentheses) are values derived by a computer program designed after our study was completed.

b After induction of anesthesia and positioning, but before the start of surgery.

c During surgery.

Table 2. Groups Based on Magnitude of Differences Between HemoCue (HCue) and Laboratory Co-Oximeter (tHb) Hemoglobin Concentration (g/dL)

<table>
<thead>
<tr>
<th>Group</th>
<th>&lt;0.5 g/dL</th>
<th>0.5–1.0 g/dL</th>
<th>1.1–1.5 g/dL</th>
<th>1.6–2.0 g/dL</th>
<th>$&gt;2.0$ g/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial (HCue – tHb) a</td>
<td>15</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>All other (HCue – tHb) a</td>
<td>50</td>
<td>7</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>65</td>
<td>12</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

a After induction of anesthesia, but before surgical incision.

b During surgery.
measures, were −3.24 and 3.77. Figure 3 displays the Bland–Altman plot of the relationship between the observed differences and the mean of the 2 measures. The horizontal dashed lines correspond to the estimated bias and limits of agreement. The data are further divided into those with a perfusion index (PI) either <1.4 (black dots) or ≥1.4 (gray dots).

The SpHb – tHb values were not systematically related to either patient age or weight. However, the variability of the SpHb – tHb differences tended to decrease with increasing duration of surgery and anesthesia (data not shown). The overall variability and absolute differences in SpHb – tHb values also were observed to decrease with increasing PI (Fig. 5), although these effects were only apparent for values of PI >4.0. Trend testing revealed that the observed differences were significantly associated with log-transformed values of tHb ($P = 0.03$), confirming the nonlinearity that is evident in Figure 5. The Bland–Altman plot in Figure 3 further identifies individual measurements according to corresponding PI values of <1.4 or ≥1.4. Conversely, underestimation by SpHb appears to be more common for measurements with PI <1.4. The difference in the average absolute differences between SpHb and tHb in the 2 groups defined by PI values of <1.4 or ≥1.4 was not statistically significant. For PI values larger than 4.0, average absolute differences were significantly smaller than were average differences for PI values <4.0. However, relatively few measurements were made for PI values larger than 4.0.

**DISCUSSION**

By providing additional and continuous data, SpHb monitoring may facilitate transfusion management. To reflect the tHb clinically, how accurate does the SpHb need to be? We propose that being within ±1.5 g/dL of the tHb value would be sufficiently accurate. Although more than half of the patients’ measurements met this benchmark, some did not. Specifically, we found that 48 (61%) of the absolute differences between SpHb and tHb were ≤1.5 g/dL. However, on the other side of the spectrum, 17 (22%) of the values were >2.0 g/dL (Table 1). Figure 2 provides complementary information on absolute differences expressed as a percentage of tHb values. From the error analysis grid in Figure 2, we conclude that 79% of SpHb measurements were within 20% of corresponding tHb values, and 39% were within 10%. HCue uniformly met our definition of being sufficiently accurate.
When comparing a new measuring device, such as SpHb, with a standard technique (e.g., tHb), variability of data from tHb should be considered. Several physiologic variables such as body position, blood source (e.g., arterial vs. peripheral venous), and time may influence the accuracy of tHb.\textsuperscript{13,14-15} To eliminate some of these variables, we used the same sampling site (radial artery), time, and body position (prone) in all patients. The overall variability for the measurement of tHb in our Medical Center’s central laboratory is consistently small (coefficient of variation: 0.8%-1.0%).\textsuperscript{13} Hospitals are required to intermittently confirm the variability of their measurement techniques.

In addition to understanding the reproducibility of the tHb, we also evaluated the accuracy of the HCue. The accuracy of the HCue has been studied previously.\textsuperscript{5} Under the conditions of our study, the HCue and tHb concentrations are virtually interchangeable (Table 2). However, measurements in our study were from arterial blood samples. Had the samples been from peripheral venous blood samples, the results may not have been so consistently similar to laboratory Co-Oximeter readings.\textsuperscript{14,15}

We observed an apparent relationship between the accuracy and variability of the SpHb and the PI (Fig. 5). Accuracy increased and variability decreased with higher PI values, with this effect being most apparent for PI values exceeding 4.0. The PI is a numerical value that has been added to the pulse oximeter. Plethysmographic pulse wave monitoring and amplitude are the basis upon which the PI is calculated. For the SpHb, the waveform and amplitude are converted into a numerical value that is displayed by the SpHb and is assumed to reflect the perfusion of the finger. The manufacturer (Masimo) recommends not using the SpHb values clinically when PI <1.4. Our results indicate that both magnitude and variability of observed differences in the 2 measurements persisted at a similar level up to PI values of at least 4.0 (Fig. 3). This increased (and unpredictable) variability associated with a lower PI supports the recommendation to not use SpHb to guide clinical decisions under these circumstances, and suggests that a higher cutoff value may be required to ensure reduced error and variability of measurements.

Finally, although the data analysis used in the study was based on the currently clinically used and available software version, we also retrospectively compared our data with data using a new software version (RevF). The data from RevF are in parentheses in Table 1. The conclusions regarding the relationships described in Figures 3 to 4 are the same using either software version.

We conclude that SpHb could have frequently been used in many patients to guide clinical decisions regarding the need for blood transfusions. In some cases, the continuous measurement can also guide the timing of direct Hb measurement using either Co-Oximetry (tHb) or point-of-care (HCue) measurements. Yet our study indicates that SpHb may not be as accurate as is clinically necessary in some patients. Our data document the need for better refinement of the noninvasive technology to address some clinically important requirements. For example, we demonstrated, not surprisingly, that peripheral perfusion is an important requirement for obtaining reliable noninvasive SpHb data. When perfusion diminishes, SpHb underestimates true Hb, so it should not be used to determine the need for blood transfusions without validation using a direct measurement methodology. As perfusion improves, the SpHb becomes a more accurate measurement methodology. PI, therefore, is as useful a clinical guide as is the actual SpHb measurement. Less obvious, but still clinically critical to understand, is why at lower Hb levels, even with good perfusion, the SpHb tends to overestimate the actual Hb level. As a result, the SpHb is an important addition to clinical monitoring as long as the current limitations are understood and addressed. As the technology improves, we may gain better insights into the relationship between perfusion, acute changes in Hb, and intravascular volume on the performance of this noninvasive monitor. It could become a standard monitor to assess patients at risk for bleeding and to guide transfusion therapy.