**Prediction of Plasma Hemoglobin Concentration by Near-Infrared Spectroscopy**

The estimation of plasma hemoglobin concentration (Hb) is among one of the daily activities in the practice of clinical anesthesiology. The near-infrared spectroscopy of the brain (rSO_2_) represents a balance between cerebral oxygen delivery and consumption. This study was designed to assess the value of rSO_2_ in the prediction of the Hb level while other variables were mathematically controlled. Thirty healthy adult patients undergoing spine surgery, expected to have a moderate degree of intraoperative bleeding, were enrolled in this study. General anesthesia was given and ventilation was mechanically controlled. Measurement of Hb and PaCO_2_ were performed at random periods of time. We obtained a total of 97 data combinations for the 30 study patients. The Hb was regressed by independent variables including rSO_2_ and PaCO_2_. A multilinear regression analysis was performed and the final regression equation was expressed only with statistically significant variables. The measured Hb was tightly regressed with three variables. The final regression equation was Hb = +8.580 + 0.238rSO_2_ - 0.338PaCO_2_ - 0.004.anesthetic exposure duration (Tmin) (p<0.000, r=0.809). Near-infrared spectroscopy was shown to be a valuable predictor of plasma Hb in the clinical anesthesiology setting.

**Key Words:** Spectroscopy, Near-Infrared, Hemoglobins; Noninvasive Monitoring

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**INTRODUCTION**

Bleeding is inevitable during most surgical procedures and estimation of the amount of bleeding is an important part of an anesthesiologists’ daily work. Anesthesiologists tend to depend on their own educated guess as an index for estimating the amount of blood loss. The plasma hemoglobin concentration (Hb) represents a standard measurement that is used to estimate blood loss and the current status of oxygen carrying capacity of arterial blood. Measurement of Hb is costly and takes a few minutes. At times, time-delay can interfere with patient management.

Research on a noninvasive in vivo estimation of Hb is very limited. In addition, the utility of any methods studied frequently requires unfamiliar instrument (1-3) or is applicable to very specific situations (4-6). We have assessed the Hb value as a factor that influences near-infrared spectroscopy referred to as cerebral oximetry, and abbreviated as rSO_2_ during a series of clinical investigations using cerebral oximetry. rSO_2_ is a well known important variable used to predict oxygen balance in the brain. We postulated that rSO_2_ would indicate Hb levels when the cerebral metabolic rate and cerebral blood flow were assumed to be constant.

Our attempt to predict Hb noninvasively was based on a simple assumption. The values of rSO_2_ represent regional cerebral field oxygen saturation; these values can be confounded by several factors such as arterial oxygen saturation (SaO_2_), arterial carbon dioxide tension (PaCO_2_), and Hb levels. We have evaluated the potential usefulness of rSO_2_ to predict Hb levels by controlling and excluding the confounders. This study was designed to test our assumption that changes in the rSO_2_ can predict changes in the Hb level when PaO_2_ and PaCO_2_ are constant, and to provide a mathematical model that demonstrates the correlation of rSO_2_ with Hb levels during general anesthesia.

**MATERIALS AND METHODS**

After approval from the Institutional Ethics Committee, we recruited thirty, American Society of Anesthesiologists (ASA) physical status I or II, adult patients (Table 1) who were scheduled for elective spine surgery, with an expectation of a moderate degree of intraoperative bleeding (20-30% of estimated blood volume). Patients with cardiovascular, endocrine or cerebral disease were excluded. General anesthesia was induced with intravenous administration of propofol (1.5 mg/kg) and vecuronium (0.1 mg/kg) and inhalation of isoflurane via a face mask. The trachea was intubated and ventilation was mechanically controlled. Anesthesia was...
maintained with isoflurane and 50% oxygen with air and intermittent administration of vecuronium. An emitter-sensor couplet of a cerebral oximeter was attached to the right forehead.

Blood loss was estimated by naked eyes. The amount of homologous blood transfusion was not regulated but performed by in-hospital protocols. Average 2-4 repeats of blood samplings in a patient for the measurement of Hb and PaCO₂ were performed by anesthesiologist’s subjective judgment at irregular periods. Full arterial oxygen saturation was confirmed at every period. At the time of skin closure, the amount of blood loss was guessed by an experienced anesthesiologist, unaware of the purpose of this study. Measured Hb and PaCO₂ were recorded alongside of rSO₂, esophageal temperature (TESO), potency of vapor anesthetic (ExpSO₂; expired concentration of isoflurane), mean arterial pressure (MAP) and anesthetic exposure duration expressed by minutes (Tmin).

Statistical analyses

Total 97 data combinations in 30 patients were obtained. Measured Hb (Hb) was analyzed by independent variables such as rSO₂, PaCO₂, TESO, MAP, Tmin, sex, age and ExpSO₂. Sex data were also included as a dummy variable. Multilinear regression analysis was performed. Variables were selected by a stepwise method and final regression equation was expressed only with statistically significant variables. Standardized residuals (sR=predicted Hb-Hb) of final regression equation were also calculated. sR were compared with zero by one-sample t-test (z-test) then smoothed by locally weighted scatterplot smoothing (lowess) technique (7). Linear regression analyses were performed between Hb and sR, and between smoothed Hb (sHb) and sR (ssR).

All statistical tests were performed using S-PLUS 8.0 for Windows (Insightful Corp, Seattle, WA, U.S.A.). The lowest parameter f was chosen to be 0.2 as a practical choice considering our sample size (7). Statistical significance of all inferential statistics was judged when \( p<0.05 \) and goodness-of-fit tests were considered to be passed when \( p \geq 0.05 \).

RESULTS

Hb, MAP, TESO, rSO₂, ExpSO₂, PaCO₂, and estimated blood loss (EBL) were recorded (Table 2). Hb was tightly regressed with three variables. Resultant regression equation was proved as follows (\( p=0.000, r^2=0.809 \)):

\[
Hb = +8.580 + 0.238 \cdot rSO₂ - 0.338 \cdot PaCO₂ - 0.004 \cdot Tmin
\]

(Eq. A)

Ignoring the minute contribution of Tmin (substituting Tmin with mean Tmin), equation A can be simplified as follows:

\[
Hb = +8.332 + 0.238 \cdot rSO₂ - 0.338 \cdot PaCO₂
\]

(Eq. B) (Fig. 1)

Standardized residuals between Hb and predicted Hb were 0.086 ± 1.100 gm/dL (\( p=0.443 \)) and were regressed by Hb

**Table 1. Patient characteristics**

|                |     |
|----------------|-----|
| N              | 30  |
| Sex (M/F)      | 15/15 |
| Age (yr)       | 44±13 |
| Body weight (kg)| 67±9  |
| Height (cm)    | 165±8.4 |
| Hb at ward (gm/dL)| 12.9±1.3 |
| MAP at ward (mmHg)| 91±12 |
| Surgical duration (min)| 146±32 |

Data are stated as mean±SD except sex distribution. 
Hb, hemoglobin concentration; MAP, mean arterial pressure.

**Table 2. Basic measurements during surgical procedures**

|                | Mean±SD | Median | Min-max |
|----------------|---------|--------|---------|
| MAP (mmHg)     | 89±10   | 89     | 58-110  |
| HR (/min)      | 74±11   | 72     | 56-112  |
| Hb (gm/dL)     | 10.8±2.0| 10.8   | 6.7-15.0|
| PaCO₂ (mmHg)   | 35.5±2.9| 35.5   | 30.4-43.0|
| rSO₂ (%)       | 61±6.6  | 60     | 49-75   |
| Tmin (min)     | 62±52   | 60     | 0-185   |
| ExpSO₂ (vol%)  | 0.8±0.1 | 0.9    | 0.6-1.2 |
| TESO (°C)      | 35.3±0.6| 35.4   | 33.8-36.2|
| EBL (ml)       | 800±400 | 775    | 250-1,750|

EBL was presented by increment of 50 mL. 
MAP, mean arterial pressure; HR, heart rate; Hb, hemoglobin concentration; PaCO₂, arterial partial pressure of carbon dioxide; rSO₂, regional cerebral oxygen saturation of right forehead; Tmin, anesthetic exposure duration; ExpSO₂, expired concentration of isoflurane; TESO, esophageal temperature; EBL, estimated blood loss.

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**Fig. 1.** Multilinear regression analysis of Hb by rSO₂ and PaCO₂. Regression equation was \( Hb=+8.332+0.238 \cdot rSO₂-0.338 \cdot PaCO₂ \) (\( p=0.000, r^2=0.809 \)). Changes of rSO₂ and PaCO₂ reflected the changes of Hb.
as follows ($p=0.000$, $r^2=0.20$):

\[ sR = -2.7705 + 0.2492 \cdot Hb \]

However, goodness-of-fit test for above equation was failed ($p=0.0274$). Lowess was performed (Fig. 2). Regression equation of lowess'ed pairs of residuals ($sR$) and $Hb$ ($sHb$) was proved as follows ($p=0.000$, $r^2=0.14$):

\[ ssR = 0.9730 - 0.1032 \cdot sHb \text{ (Eq. C)} \]

Test statistic for goodness-of-fit of equation C was 0.6877 (Fig. 3).

**DISCUSSION**

In this study, we evaluated whether rSO$_2$ could predict the true or measured $Hb$ levels using a prediction equation that was compared with clinically relevant levels of measured $Hb$. We successfully derived a mathematical equation that showed a correlation of $Hb$ and rSO$_2$. Arterial carbon dioxide tension and anesthetic duration also affected the predicted $Hb$ levels. Other potential variables that could affect the equation were excluded or included by stepwise selection. By the analysis of the residuals according to the measured $Hb$ levels, the predicted $Hb$ level by equation A had a tendency to underestimate the $Hb$ level when the measured $Hb$ levels were high, and to overestimate the $Hb$ level when the hematocrit was low. Interestingly, our results are consistent with the classical concept of an inverse correlation between cerebral blood flow and hematocrit in animals (8, 9) and humans (10). For the level of measured $Hb$ that appears to be a cut-off point for overestimation was 9.4 gm/dL ($0.9730/0.1032$ from equation C). We predict that 1) low $Hb$ below 9.4 gm/dL causes the cerebral vessels to dilate and raises the rSO$_2$, and 2) high $Hb$ over 9.4 gm/dL may impede cerebral blood flow and lowers rSO$_2$ thereby lowers the predicted $Hb$ level.

Arterial carbon dioxide tension is another important variable that affects the result of our equation, and also a potential confounding factor, which made Dullenkopf et al. (11) fail to prove the relationship of rSO$_2$ and $Hb$. We believe that an anesthesiologist can manage the arterial carbon dioxide tension within 5 mmHg, which affects $Hb$ level $\pm 1.6$ gm/dL ($5 \times 0.338$ from equation A).

Anesthetic duration also affects the equation. Most vapor anesthetics increase cerebral blood flow (CBF) initially but decrease CBF to a steady state near pre-exposure levels in animals (12). This finding was not evident in humans (13).
Our results show that prolonged exposure of isoflurane caused small increases of rSO2. This finding is not consistent with previous reports (12, 13). Possible explanation includes the inevitable failure of statistical independence of time-effect; the measured Hb decreases as a function of time in every patient. However, our result confined the time-effect within 0.004; this would suggest that the rSO2 increased spontaneously up to +1% during 180 min of anesthesia despite a steady state of Hb; therefore, the time effect can be ignored in clinical decisions.

Our findings are compatible with the basic understanding on cerebral physiology and rheology. However, we do not suggest that our equation should be used to predict Hb levels for everyday anesthesia procedures; but rather provide additional information to better understand noninvasive prediction of Hb levels. Potential bias should be eliminated by further studies with a controlled study design and larger clinical database.

In conclusion, the value of near-infrared spectroscopy, rSO2 as an accurate, easy-to-read, noninvasive, real-time, and continuous predictor of Hb levels in clinical anesthesia has been demonstrated in this study. PaCO2 and anesthetic duration should also be considered as important factors for predicting Hb by rSO2. The Hb levels tend to be overestimated at lower Hb levels with the model presented here. Users of this model should keep in mind the assumptions of this design which includes a normal cerebral vasculature and blood pressure.

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