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ORIGINAL ARTICLE

The accuracy of non-invasively continuous total hemoglobin measurement by pulse CO-Oximetry undergoing acute normovolemic hemodilution and reinfusion of autologous blood

Junichi Saito · Masato Kitayama · Masafumi Oishi · Tomoyuki Kudo · Masahiro Sawada · Hiroshi Hashimoto · Kazuyoshi Hirota

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Abstract

Background Non-invasively continuous total hemoglobin (SpHb) measurement has not been assessed adequately in acute bleeding and rapid blood transfusion during surgery. Thus, we have assessed the efficacy of SpHb during both acute normovolemic hemodilution (ANH) and autologous blood transfusion (ABT).

Methods Twenty-four patients undergoing urological and gynecological surgery were enrolled. ANH was induced by withdrawing blood of 800 g with simultaneous fluid administration. When surgical hemostasis was completed, collected blood was reinfused. Measurement of SpHb, perfusion index (PI) and real total Hb (tHb) were done before and after each 400 ml blood removal (−0, −400, −800 ml) and reinfusion (+0, +400, +800 ml).

Results A Bland–Altman analysis for repeated measurements showed a bias (precision) g/dl of 1.12 (1.25), 1.43 (1.24) and 1.10 (1.23) for all data, during ANH and during ABT, respectively. Additionally, a bias (precision) increased with a reduction in tHb (g/dl): ≥10.0; 0.74 (1.30), 8.0–10.0; 1.15 (1.12) and <8.0; 1.60 (1.28). Although the difference between SpHb and tHb was almost zero before anesthesia induction, it became significant just before ANH and did not change further by ANH and ABT. Significant correlations between SpHb and tHb for all data ($r = 0.75, n = 228, p < 0.001$) were observed. PI slightly correlated with the difference between SpHb and tHb ($r = 0.38$, $n = 216, p < 0.001$). Furthermore, before and after induction of anesthesia, PI also correlated with the difference between SpHb and tHb ($r = 0.42$, $n = 23$, $p = 0.048$ and $r = 0.51$, $n = 22$, $p = 0.016$, respectively).

Conclusions The present data suggest that SpHb may overestimate tHb during ANH and ABT. In addition, PI and tHb levels had an impact on the accuracy of SpHb measurements.

Keywords Hemoglobin · Hemodilution · Autologous blood transfusion

Introduction

Measurement of hemoglobin (Hb) concentration is essential to assess the need for blood transfusion during surgery. Repeated blood samplings are sometimes required to assess changes in the Hb level during major surgery. However, delay of blood transfusion and severe anemia may occur during active bleeding with time-consuming laboratory measurement. Thus, continuous measurement of Hb is desirable. Recently, a non-invasive and continuous total hemoglobin (SpHb) measurement device was developed,

J. Saito (✉) · M. Kitayama · M. Oishi · T. Kudo · M. Sawada · K. Hirota
Department of Anesthesiology, Hirosaki University Graduate School of Medicine, Hirosaki 036-8562, Japan
e-mail: fix-you@hotmail.co.jp

M. Kitayama
e-mail: masuika@cc.hirosaki-u.ac.jp

M. Oishi
e-mail: Skdjg633@yahoo.co.jp

T. Kudo
e-mail: kudotomoyuki@yahoo.co.jp

M. Sawada
e-mail: daoyandz@yahoo.co.jp

K. Hirota
e-mail: hirotak@cc.hirosaki-u.ac.jp

H. Hashimoto
Division of Surgical Center, Hirosaki University Hospital, Hirosaki, Japan
e-mail: hasimoto@cc.hirosaki-u.ac.jp

and its efficacy has been reported in the several clinical settings including surgical and intensive care patients [1–3]. However, this non-invasive technology has not been assessed adequately in acute bleeding and/or rapid blood transfusion which would make for relatively rapid change of Hb levels during surgery.

The purpose of acute normovolemic hemodilution (ANH) with retransfusion of autologous blood transfusion (ABT) is to avoid or limit allergenic blood transfusion [4]. ANH is induced with acute withdrawing of 400–1200 g that is replaced by an appropriate volume of crystalloids or artificial colloids to maintain circulating volume [4]. Then, the ABT is performed either intraoperatively or after surgery. Indeed, previous clinical studies revealed that ANH with ABT reduced the number of patients avoiding exposure to allogeneic blood undergoing major liver surgery, radical prostatectomy, and cardiac surgery [5–7]. On the basis of these data, we often perform ANH and ABT as standard practice for urological and gynecological surgeries, which may have over 1000 ml of blood loss.

In the present study, we have prospectively assessed the efficacy of SpHb in patients undergoing urological and gynecological surgery during both ANH and ABT, which would make for relatively rapid change of Hb levels.

Methods

This study protocol was approved by our University ethic committee and was registered in a publicly accessible database, the UMIN Clinical Trial Registry, which is one registry of the Japan Primary Registries Network (UMIN000006886). We enrolled patients with written informed consent who were scheduled to undergo urological or gynecological surgery under general anesthesia with the ANH and ABT technique at Hirosaki University hospital. Patients who were so categorized were enrolled in this study. Exclusion criteria were Hb <10 g/dl, a past history of ischemic heart disease, central nervous system diseases, and/or ASA physical status ≥ III.

Monitoring

Upon arrival in the operating room, all patients were attached to ASA standard monitors and had a bispectral index (BIS), and an invasive arterial blood pressure taken. In addition, a non-invasive hemoglobin monitor, the Rainbow adult ReSposable™ sensors were attached at the ring fingertip, contralateral to the invasive arterial catheter, and then connected to a Radical-7 Pulse CO-Oximeter (SET version 7601; Masimo Corporation, Irvine, CA, USA). The sensors were covered with a black plastic shield to prevent optical interference.

Anesthesia

Anesthesia was induced with propofol (1–1.5 mg/kg), remifentanil (0.2–0.5 μg/kg/min), and ketamine (0.4–1.0 mg/kg). Neuromuscular blockade was established with rocuronium (0.6–1.0 mg/kg) to facilitate endotracheal intubation. Anesthesia was maintained with propofol (3–6 mg/kg/h), remifentanil (0.1–0.5 μg/kg/min), and ketamine (0.1–0.2 mg/kg/h) to maintain a BIS monitoring of 40–60. A blood sampling from the radial artery catheter was performed to obtain the real Hb concentration. Then, central venous catheterization via the internal jugular vein was performed to monitor pressure monitoring and withdraw blood and do infusion of fluid and blood.

ANH and ABT procedure

The ANH was induced by withdrawing 800 g of whole blood into standard blood collection packs containing citrate phosphate dextrose solution and the simultaneous administration of 1000 ml of lactate Ringer's solution including 3 % dextrane-40 (Saviosol®, Otsuka Pharmaceutical Co., Tokyo, Japan) to maintain normovolemic state. Patients also continuously received acetate Ringer's solution throughout anesthesia. When surgical hemostasis was completed, collected blood was rapidly reinfused to the patients.

Data collection

Measurement of the SpHb, perfusion index (PI), plethysmographic variability index (PVI), and real total Hb (tHb) were done before and after each 400 ml blood removal (−0, −400, −800 ml) and reinfusion (+0, +400, +800 ml) and every 30 min during surgery. Arterial blood samples were simultaneously collected to measure tHb with a KX-21N Hematology Analyzer (Sysmex Corporation, Kobe, Japan).

Data analysis

The relationships between variables were examined using Pearson's correlation coefficient and a least squares linear regression line that was fitted using GraphPad Prism V3 (GraphPad Software Inc., CA, USA). Bias was defined as the difference between SpHb and tHb and precision was defined as 1 SD of the bias. We also did a Bland–Altman analysis to compare SpHb with tHb over the range of values. This statistical method was used to estimate the bias and precision for all data, before induction of anesthesia, during ANH, during ABT, tHb ≥10.0 g/dl, 8.0 g/dl ≤ tHb < 10.0 g/dl, and tHb <8.0 g/dl. All data are presented as the mean ± SD. For measurements repeated over time, a mixed models analysis of variance (ANOVA) was used to determine whether statistically differences were present across each sampling point. The Neuman–Kreuls test was used for post hoc analysis to determine the specificity of the changes at each sampling point compared with all sampling points. A p value under 0.05 was considered significantly different.

Table 1 Characteristics of patients and surgical procedures

Patients	$n = 24$
Male/female	17/7
Age (years)	61 ± 12
Height (cm)	161.4 ± 8.1
Preoperative body weight (kg)	60.9 ± 7.5
Operation time (min)	142 ± 53
Anesthesia time (min)	201 ± 54
Estimated blood loss (g)	573 ± 374
Surgical procedures	
Radical prostatectomy	13
Nephrectomy	4
Radical hysterectomy	3
Semiradical hysterectomy	4

Data are expressed as mean ± SD

Results

Twenty-four patients were enrolled in this study. Demographic data are shown in Table 1. The ANH and ABT protocol were completed in all of the patients, even though a male patient whose tHb was 10.7 g/dl just before induction had removed only 400 ml not 800 ml. No patient received the allogeneic transfusion throughout the study period. A total of 228 blood samples were drawn and evaluated for tHb. A mean of 9 samples was collected per patient.

A Bland–Altman analysis of all data is shown in Fig. 1a. Mean bias (precision) of 228 SpHb and tHb values were 1.12 (1.25) g/dl. The same analysis for the measurement at before induction of anesthesia, during ANH, and during ABT showed a bias (precision) of −0.10 (1.08) g/dl (Fig. 1b), 1.43 (1.24) g/dl (Fig. 1c), and 1.10 (1.23) g/dl (Fig. 1d). Additionally, a bias (precision) increased with a reduction in tHb: tHb ≥10.0 g/dl, 0.74 (1.30) g/dl, 8.0 g/dl ≤ tHb < 10.0 g/dl, 1.15 (1.12) g/dl, tHb <8.0 g/dl, and 1.60 (1.28) g/dl, respectively.

Significant correlations between SpHb and tHb were observed during all of the study period (Fig. 2).

Data of the SpHb and tHb difference between SpHb and tHb (SpHb − tHb) and PI and PVI are presented in Table 2. Both SpHb and tHb were significantly decreased

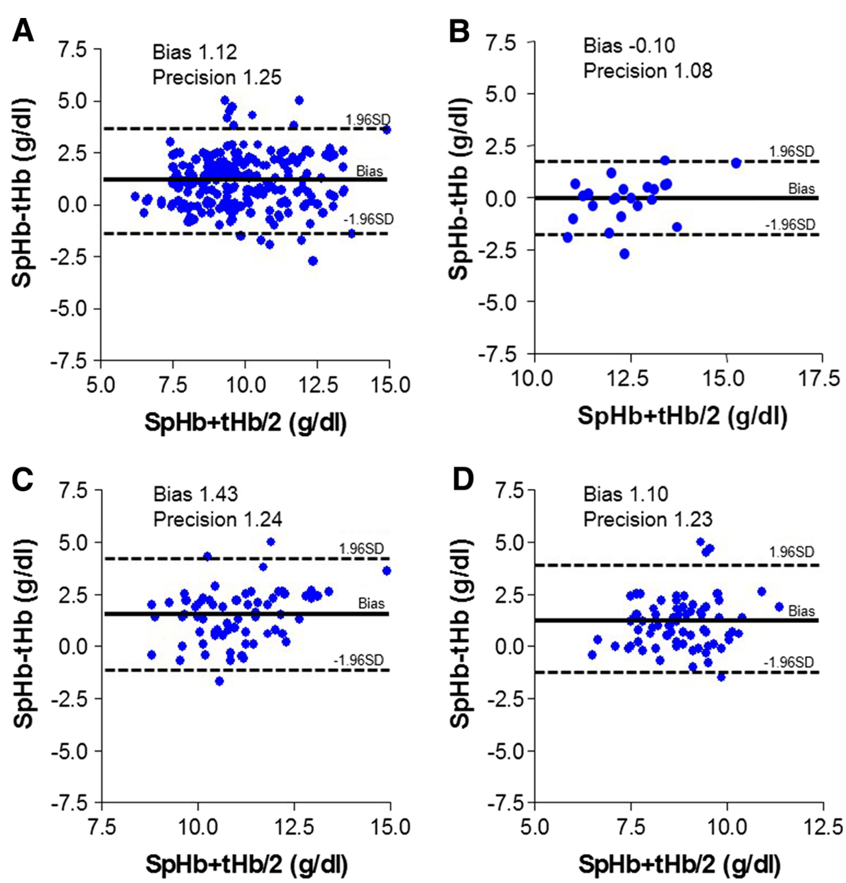

Fig. 1 The Bland–Altman analysis of the bias and precision to compare non-invasive with invasive measurements of hemoglobin concentration for all data (**a**), data before induction of anesthesia (**b**), data during acute normovolemic hemodilution (**c**) and data during autologous blood transfusion (**d**)

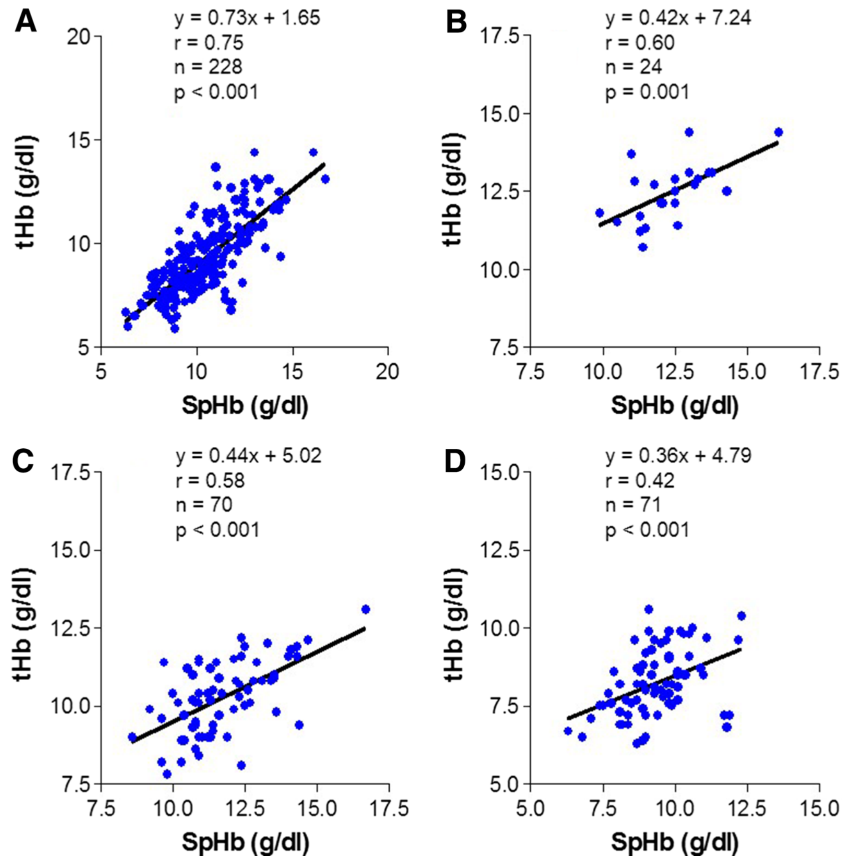

Fig. 2 The relationship between non-invasive and invasive measurements of hemoglobin concentration for all data (**a**), data before induction of anesthesia (**b**), data during acute normovolemic hemodilution (**c**) and data during autologous blood transfusion (**d**)

Table 2 Changes in variables by anesthesia, hemodilution and autologous blood transfusion

	Before induction	Acute normovolemic hemodilution			Autologous blood transfusion		
		−0 ml	−400 ml	−800 ml	+0 ml	+400 ml	+800 ml
SpHb (g/dl)	12.3 ± 1.3	12.6 ± 1.4	11.6 ± 1.3[a]	10.7 ± 1.0[a]	9.2 ± 1.2	9.2 ± 1.2	9.5 ± 1.1
tHb (g/dl)	12.4 ± 0.9	11.1 ± 0.9	10.2 ± 0.8[a]	9.4 ± 0.9[a]	8.0 ± 0.9	8.1 ± 1.0	8.5 ± 1.1
SpHb − tHb (g/dl)	−0.1 ± 1.0	1.5 ± 1.2[b]	1.4 ± 1.2[b]	1.3 ± 1.2[b]	1.2 ± 1.0[b]	1.1 ± 1.2[b]	0.9 ± 1.3[b]
PI (%)	3.6 ± 1.7	5.6 ± 2.3[c]	3.5 ± 1.7	2.7 ± 1.4	2.6 ± 1.4	2.3 ± 1.3	2.5 ± 1.3
PVI	NA	12.7 ± 5.7	15.4 ± 6.0	19.6 ± 8.8[c]	17.3 ± 6.5	16.2 ± 6.8	17.0 ± 8.6

SpHb hemoglobin concentration measured by non-invasive monitor, *tHb* total hemoglobin concentration measured in laboratory, *PI* perfusion index, *PVI* plethysmographic variability index

[a] A significant difference from just before acute normovolemic hemodilution (−0 ml), Neuman–Kreuls test

[b] A significant difference from before induction of anesthesia, Neuman–Kreuls test

[c] A significant difference from before induction of anesthesia, Neuman–Kreuls test

by ANH, respectively, whilst both variables did not change by ABT. Interestingly, although the difference between SpHb and tHb was almost zero before induction of anesthesia, it became significant just before ANH and did not change further by ANH and ABT. Both PI and PVI were significantly decreased and increased by ANH, respectively, whilst both variables did not change by ABT. PI slightly correlated with SpHb − tHb (Fig. 3a), but PVI did not. Furthermore, before and after induction of anesthesia, PI significantly correlated with SpHb − tHb (Fig. 3b, c).

Discussion

In this study, we have examined the relationship between SpHb and tHb during ANH and ABT. The present data demonstrated that SpHb significantly overestimated the Hb concentration after induction of anesthesia and during ANH and ABT.

During surgery, several factors, not only vascular tone but also Hb level and/or intravascular volume, could change every moment, so which factors could affect the

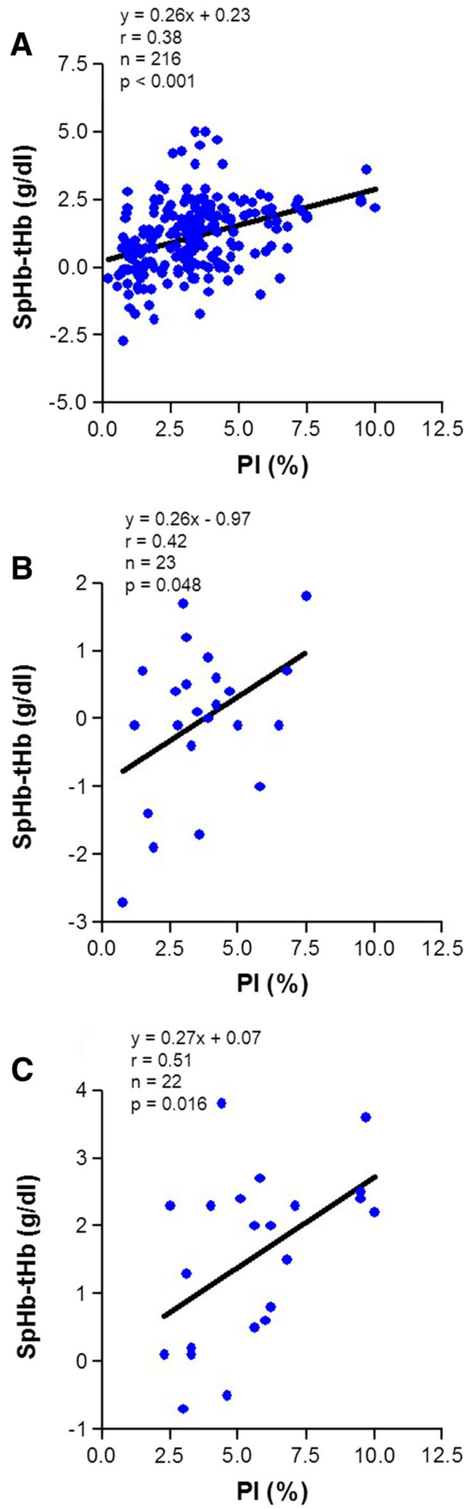

Fig. 3 The relationship between perfusion index and the difference between non-invasive and invasive measurements of hemoglobin concentration for all data (**a**), before (**b**) and after (**c**) induction of anesthesia

accuracy of the measurement was difficult to specify. General anesthesia induces vasodilation with a reduction in sympathetic tone without major change of Hb levels and intravascular volume. So induction of anesthesia is a suitable situation to assess an impact of the PI on the accuracy of SpHb measurement. It has been reported that PI would increase by regional anesthesia that produces sympatholytic effects [8, 9]. Indeed, PI values were significantly increased after induction of anesthesia compared with those before induction of anesthesia, and mean SpHb − tHb values were also increased after induction of anesthesia (Table 2). Furthermore, PI had significant correlations with SpHb before and after induction of anesthesia (Fig. 3b, c). These results suggested that PI had an impact on the accuracy of SpHb measurements.

The accuracy of the SpHb measurement has been assessed under several clinical conditions, including patients undergoing surgery and in the intensive care units [2, 10–15]. Causey and colleagues [11] reported that a SpHb bias was 0.29 g/dl with a 95 % confidence interval of −0.09 to 0.50 and a correlation coefficient of 0.78 when compared with tHb in patients undergoing major surgery. Lamhaut and colleagues [13] found that a SpHb bias (precision) was −0.02 (1.39) g/dl and the correlation coefficient was 0.77 in patients undergoing urological surgery. The present data are similar to these data as an overall correlation coefficient was 0.75 although our SpHb bias was higher than theirs.

There is a single report [1] showing that SpHb measurement was accurate compared with laboratory tHb in conscious healthy volunteers undergoing hemodilution [with a bias (precision) of −0.15 (0.94) g/dl]. In the present study, SpHb overestimated tHb after induction of anesthesia, during ANH and ABT. As described above, an increase in PI following induction of anesthesia may increase the bias. Moreover, Vos and colleagues [15] found that the accuracy of SpHb measurement decreased during colloid administration in the dynamic phase undergoing liver surgery. Their results suggest that a colloid solution may affect the accuracy of SpHb measurement. The reason is not clear, however, and the difference of hemoglobin concentration between microcirculation and macrocirculation might have a significant impact on the relation between SpHb and tHb. Hemoglobin concentration in macrocirculation is usually higher than that in microcirculation in a stable condition. This is due to the reduction in hematocrit entering capillaries, known as the Fahraeus effect [16, 17]. This effect results from erythrocytes moving faster than plasma in microcirculation. However, hemoglobin concentration decreases in macrocirculation and stays essentially unchanged in microcirculation despite a significant decrease of hemoglobin concentration in macrocirculation during blood loss and hemodilution. Naftalovich and colleagues [18] claimed that misinterpretation of SpHb was exaggerated during blood loss due to the physiological phenomenon in agreement with our findings.

Therefore, SpHb may not be reliable if undergoing ANH and ABT during surgery under general anesthesia.

An important finding in this study was that the accuracy of SpHb measurement was decreased with a reduction in tHb values. Particularly, when tHb decreased to <8.0 g/dl, the bias between SpHb and tHb were the highest, compared with those at tHb $\geq$10.0 g/dl and 8.0 g/dl $\leq$ tHb $<$ 10.0 g/dl. The measured hemoglobin concentration is important for the decision to administer red blood cells. Therefore, the accuracy of the SpHb measurement for tHb <8.0 g/dl is required to avoid unnecessary blood transfusion and not to overlook necessary blood transfusion, since both situations are harmful for patients. These results suggested that the blood transfusion should not be determined by only SpHb during general anesthesia and surgical procedure.

There are some limitations in the present study. In the present study, patients underwent urological and gynecological surgery under total intravenous anesthesia using propofol, remifentanil, and ketamine. Thus, it is not certain whether our result is fully applicable to patients undergoing other types of surgery and/or anesthesia such as inhaled anesthesia. Furthermore, the sample size was small. So further studies are needed to confirm our findings.

In conclusion, the present data suggest that SpHb may overestimate tHb after induction of anesthesia, during ANH, and during ABT although SpHb could follow the changes in tHb during these procedures. Therefore, we suggest that one should carefully use the SpHb monitor during surgery especially under general anesthesia.

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Conflict of interest The author(s) declare that they have no competing interests.

Ethical standards This study protocol was approved by Hirosaki University ethic committee. Zaifu-cho 5, Hirosaki 036-8562, Japan.

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