International Journal of Laboratory Hematology
The Official journal of the International Society for Laboratory Hematology

Accuracy of noninvasive hemoglobin and invasive point-of-care hemoglobin testing compared with a laboratory analyzer

N. SHAH*, E. A. OSEA†, G. J. MARTINEZ‡

*Long Beach Veterans Administration Healthcare System, Long Beach, CA, USA
†Innovative Clinical Research, Inc., Harbor City, CA, USA
‡Catalina Research Institute, LLC, Chino, CA, USA

Correspondence:
Nitin Shah,
Professor of Anesthesiology, Department of Anesthesiology, Loma Linda University Medical Center, Chief, Surgical ICU, Long Beach Veteran's Administration Healthcare System, 5901 E. 7th St., Long Beach, CA 90822, USA.
Tel.: +562-826-8000 x3264;
Fax: +562-826-5991;
E-mail: nitinshahmd@gmail.com

doi:10.1111/ijlh.12118

Received 27 February 2013; accepted for publication 27 May 2013

Keywords
Anemia, HemoCue, hemoglobin, pulse oximetry, noninvasive

SUMMARY

Introduction: Hemoglobin concentration is assessed to detect anemia and its associated morbidities. Hemoglobin is usually determined from venous or capillary blood samples run on a laboratory analyzer. However, this method requires a needle stick and results can be delayed. It also exposes caregivers to risks associated with needle sticks and blood exposure. Noninvasive hemoglobin determination would be of benefit to patients and caregivers because it would allow for quick and painless point-of-care assessment.
Methods: Hemoglobin determination from a noninvasive spot check hemoglobin device (Pronto-7 with SpHb, Masimo) and an invasive point-of-care device (HemoCue) was compared with venous blood samples run on a laboratory hematology analyzer.
Results: A total of 440 outpatients and healthy volunteers were included (mean age 36 years, 62% female). Compared with the hematology analyzer, the bias ± standard deviation of was −0.1 ± 1.1 g/dL for SpHb and −0.1 ± 1.6 g/dL for HemoCue.
Conclusion: Noninvasive hemoglobin testing with SpHb provided similar accuracy as invasive point-of-care hemoglobin testing and may enable more efficient and effective patient care.

INTRODUCTION

Determination of hemoglobin concentration for anemia assessment is among the most frequently performed laboratory tests in inpatient and outpatient care [1]. Anemia is caused by impaired production or increased destruction of red blood cells, blood loss, or fluid overload and is often not associated with specific symptoms. Some common morbidities such as lesions and tumors in the gastrointestinal tract, gynecologic disturbances, and others can be associated with or cause anemia and may be initially diagnosed by routine hemoglobin level measurement in patients. Traditionally, hemoglobin concentration is either measured

from venous blood samples with hematology analyzers or from capillary blood samples with handheld point-of-care devices.

A spectrophotometric method to determine hemoglobin concentration using a noninvasive, multiwavelength sensor has been developed and commercialized with multiple devices by Masimo Corporation for spot check and continuous measurement applications, and as of this writing are the only noninvasive hemoglobin devices commercially available in the United States. According to the manufacturer's description of the technology, the SpHb sensor emits more than 7 wavelengths of light to acquire hemoglobin concentration data based on light absorption through the finger. Signal processing algorithms and adaptive filters translate the absorption data to quantitate hemoglobin based on an empirically derived 'look-up' table, much like conventional pulse oximetry.

Published data have focused on the use of this technology for continuous measurement of hemoglobin in hospital operating rooms and intensive care units [2–4]. In this study, we sought to compare noninvasive and an invasive spot check, point-of-care hemoglobin devices with a reference laboratory hematology analyzer in an outpatient setting to determine their accuracy.

MATERIALS AND METHODS

The study was approved by an institutional review board. Study subjects were adult and pediatric individuals presenting to two outpatient clinics and one health screening event in southern California. Following written informed consent, subject demographics and medications were recorded for each subject. The Massey and Martin New Immigrant Survey (NIS) Skin Color Scale [5] was used to categorize skin pigmentation, with light pigmentation considered to be 1–3, medium pigmentation considered to be 4–7, and dark pigmentation considered to be 8–10. Following measurement and recording of finger diameter, a noninvasive hemoglobin (SpHb) test device (Pronto-7, version 2.19, with a rainbow 4D sensor, rev E, Masimo Corp., Irvine, CA, USA) was placed on the subject's nondominant ring finger. The sensor was covered with an opaque shield to prevent optical interference. A noninvasive hemoglobin measurement was obtained from each subject. Perfusion index, finger temperature, and oxygen saturation (SpO_2), measured by the noninvasive hemoglobin test device, were also recorded. Testing was conducted while subjects were quiet and sitting upright.

Immediately following the noninvasive testing, a venous blood sample was obtained by venipuncture of the median cubital vein of the nondominant arm with a disposable syringe and then transferred to 2-mL vacuum tube containing ethylenediaminetetraacetic acid (EDTA anticoagulant). Venous blood samples were transported at room temperature and analyzed for reference hemoglobin value (Hb) with a laboratory hematology analyzer (LH 500, Beckman Coulter, Brea, CA, USA) as per Clinical and Laboratory Standards Institute guidelines [6] and the manufacture's directions for use, within 24 h of collection. The laboratory analyzer was calibrated daily as per the manufacturer's recommendations and good laboratory practice.

A capillary blood sample was also obtained by finger stick with a 2.25 finger lancet within 15 min of the noninvasive reading and the venous sample and analyzed immediately with a point-of-care hemoglobinometer (HemoCue 201 + , Hemocue, Cypress, CA, USA) according to the manufacturer's directions for use.

Accuracy of SpHb and hemoglobin by the point-of-care device (HemoCue) was assessed by calculating bias and standard deviation of each test method compared with laboratory Hb. Additionally, Bland–Altman graphs with limits of agreement were plotted to assess agreement between methods across the range of hemoglobin values [7].

Student's t-test and Levene's test for equal variances were performed to analyze the differences between the biases of the HemoCue device and the Pronto-7 compared with the reference device for subjects in several demographic subgroups.

Multiple regression analysis using a general linear model was performed to evaluate the associations of subject characteristics to SpHb–Hb bias and Hemocue–Hb bias. Variables analyzed were skin pigmentation, smoking status, health status, weight, gender, and SpO2 values.

RESULTS

Four hundred and seventy-four subjects were enrolled in the study. In 26 subjects, no venous sample was obtained, in 6 subjects, no SpHb value was obtained,

and in 1 subject, no Hemocue value was obtained. Therefore, hemoglobin results from a venous sample, SpHb, and Hemocue were obtained in 440 subjects and included in the analysis. Four hundred and three (92%) were from outpatient clinics, and 37 (8%) were from a community health screening event. The age range of participating subjects was 3 to 86 years with an average of 36 years, with 62% being female. The study population consisted of 257 (58%) healthy subjects and 183 (42%) outpatients presenting with one or more conditions. Subject demographics are shown in Table 1A and health status information in Table 1B.

The reference Hb ranged from 8.6 to 17.4 g/dL. Analysis of data from all subjects showed a bias ± standard deviation of −0.1 ± 1.1 g/dL for Pronto-7 SpHb and −0.1 ± 1.6 g/dL for HemoCue, compared with the hematology analyzer (Table 2). Bland–Altman analysis demonstrated limits of agreement of −2.3 to 2.1 g/dL for SpHb and −3.2 to 3.0 g/dL for HemoCue (Figure 1a, b).

Student's *t*-tests comparing average biases and Levene's test for equal variance of SpHb and the point-of-care device with reference laboratory hemoglobin showed no significant differences between devices in all subjects. Student's *t*-tests comparing the biases of the two methods in healthy individuals, individuals presenting with common morbidities, smoking and nonsmoking individuals, or those with light or medium to dark pigmentation also showed no significant differences between SpHb and HemoCue measurements in those respective subgroups (data not shown).

Multiple regression analysis assessing medical conditions, smoking status, Massey scale, and SpO2 revealed Massey scale to be a significant predictors of SpHb bias. For each increase in Massey scale, SpHb bias increased by 0.16 g/dL. Higher biases were observed in darker-pigmented patients (Massey scale 4–9), but the number of subjects in this group was small. No variable was found to have a significant effect on the bias of HemoCue measurements.

DISCUSSION

Hemoglobin testing is performed hundreds of million times in United States each year. Low hemoglobin values indicate anemia and initiate investigations to the cause, which can range from diet deficiencies to lesions in the gastrointestinal tract to life-threatening disorders.

Point-of-care devices with capillary devices enable immediate assessment of hemoglobin and incorporation into the clinician's diagnostic and therapeutic plan, but still require a finger stick blood sample

Table 1. Patient demographics and medical conditions for 440 patients

(A)

		Ethnicity, n (%)					Pigmentation (Massey Scale), n (%)		
Male/ Female	Average (range) Age, year	Caucasian	African American	Asian	Hispanic/ Latino	Other	Light	Medium	Dark
169/271	36 (3–86)	53 (12)	52 (12)	51 (12)	281 (64)	3 (0.7)	369 (84)	64 (15)	7 (2)

(B)

Health status, n (%)		Common morbidities, n (%)	
Healthy	257 (58%)	Diabetes	72 (16%)
Comorbidities	183 (42%)	Hypercholesterolemia	68 (15%)
BMI (avg) (±SD)	29 (±7.6)	Hypertension	32 (7%)
Smokers	57 (13%)	Asthma	21 (5%)
Nonsmokers	383 (87%)	Arthritis	17 (4%)
Pregnancy	3 (0.6%)	COPD	13 (3%)

BMI = body mass index; SD = standard deviation.

Table 2. Agreement of Pronto-7 SpHb and HemoCue to venous laboratory reference values (Hb)

	Pronto-7 Bias±SD, g/dL	HemoCue Bias±SD, g/dL
All subjects	−0.14 ± 1.1	−0.11 ± 1.6
Smokers	0.03 ± 1.1	−0.10 ± 1.9
Nonsmokers	−0.17 ± 1.2	−0.11 ± 1.5
Comorbidities	−0.02 ± 1.2	0.01 ± 1.4
Healthy	−0.23 ± 1.1	−0.19 ± 1.7
Light pigmentation	−0.23 ± 1.1	−0.11 ± 1.6
Med dark pigmentation	0.34 ± 1.2	−0.10 ± 1.4

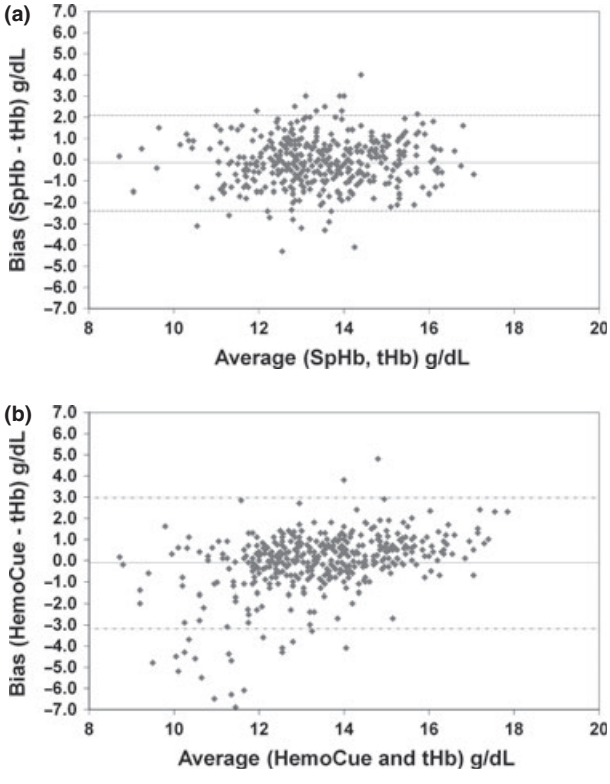

Figure 1. Bland–Altman graph of hemoglobin from Pronto-7 (SpHb) and Hemocue *vs.* laboratory reference values (Hb). Bland–Altman graph of (a) Pronto-7 (SpHb) and (b) point-of-care hemoglobin (HemoCue), compared laboratory hematology analyzer hemoglobin (Hb) for 440 subjects with solid red line indicating the bias and dotted line indicating the upper and lower 95% limits of agreement.

which is painful to the patient and exposes caregivers to bloodborne pathogens. Because both capillary and venous methods are invasive, most providers opt for venous blood sample testing, which can delay assessment and requires additional time by the provider the next day to interpret test results and communicate the test results back to the patient even when the test results are not concerning. Because a venous blood sample enables a complete blood count test to be performed and provides additional information such as white blood cell count, mean corpuscular volume, platelet count most providers order the complete blood count even when hemoglobin alone may be the only measurement needed for an initial screen for anemia. Indeed, Medicare data show that complete blood counts are performed >30 times more frequently than hemoglobin alone [8].

If it provided comparable accuracy to point-of-care devices with capillary blood, noninvasive hemoglobin measurement could provide significant advantages in the delivery of patient care, such as helping providers rule out of anemia as a cause of signs or symptoms during the office visit and provide immediate counseling to the patient. This may also increase healthcare efficiency by preventing additional office visits and reducing time to interpret next day test results. If the need for hemoglobin testing could be satisfied in the office visit, it may also alleviate venipuncture and subsequent laboratory testing for complete blood count, reducing healthcare costs. Noninvasive hemoglobin testing has been shown to increase patient satisfaction [9], an increasingly important factor in measuring healthcare quality [10].

Many clinicians do not have a complete understanding of laboratory testing methods, their limitations, and the numerous clinical circumstances that can cause variance or interference to laboratory results [11, 12]. 'The International Committee for Standardisation in Haematology reference haemoglobin method', the hemiglobincyanide (HiCN) method [13] is required by the Food and Drug Administration for laboratory device submissions but is impractical for clinical use. Hematology analyzers are considered the next best method available [14]. Hemoglobin variability between laboratory devices still exists; identical blood gas analyzers with different serial numbers have shown variability as high as 1.2 g/dL standard deviation [15]. In 50 postoperative patients, Gehring found bias of 0.3 g/dL and standard deviation of 0.2 g/dL between HiCN and a hematology analyzer and bias of −0.2 g/dL and standard deviation of 0.3 g/dL between HiCN and a

blood gas analyzer in the same patients [14]. Variation in hemoglobin measurements is most often due to preanalytic errors however, which may include clotting, contamination, delay in processing the sample, or other errors in collection and processing [12]. These findings indicate that hemoglobin concentration measurements are subject to numerous source of variation, which, while well understood by the laboratorian, may not be appreciated by the average clinician [12], but nevertheless should be taken into account when evaluating a new method of measurement.

Continuous and noninvasive hemoglobin testing with the SpHb spectrophotometric method has been clinically evaluated in multiple studies in hospital operating rooms and intensive care units [2–4] with some studies also comparing HemoCue measurements with the reference device [16]. Many of these studies have found acceptable accuracy and precision of SpHb measurement in comparison with laboratory hematology analyzers or CO-Oximeters. Berkow *et al.* [2], for example, evaluated the accuracy of continuous SpHb monitoring compared with laboratory CO-Oximetry in 29 complex spine surgery patients and found an absolute bias and standard deviation of 0.8 ± 0.6 g/dL. Lamhaut *et al.* [16], found a bias and standard deviation of SpHb to be 0.2 ± 1.1 g/dL from 85 paired measurements (hematology analyzer reference) from 44 patients undergoing major urologic surgery, whereas the bias and standard deviation for HemoCue was −0.2 ± 0.8 g/dL in the same patients. Frasca *et al.* [4] studied continuous SpHb and spot check HemoCue measurements compared with measurements from a hematology analyzer from 62 intensive care patients and found bias and limits of agreement of 0.0 ± 1.0 g/dL for SpHb and 0.3 ± 1.3 for HemoCue. There are very few studies that have evaluated noninvasive spot check devices. Gayat *et al.* [9], compared hemoglobin measurement from the Pronto-7 spot check device and another noninvasive spot check device, the Orsense NMB-200M, with a hematology analyzer in emergency room patients and found a larger standard deviation than we report in this study (±1.2 g/dL) but smaller standard deviation than the Orsense device (1.6 g/dL). Raikhel [17] tested the Pronto (another spot check device from Masimo) and HemoCue compared with hematology analyzer in 152 patients from a single outpatient center and found similar results to this study with biases and standard deviations of 0.5 ± 1.0 g/dL for SpHb and 0.3 ± 1.0 for HemoCue. Here, we present the first multisite study assessing the performance of noninvasive hemoglobin spot check measurement from the Pronto-7 in the outpatient clinic environment.

In our study comparing noninvasive SpHb from the Pronto-7 and point-of-care device hemoglobin from HemoCue with a laboratory hematology analyzer, we showed that the noninvasive method performs with similar accuracy as the point-of-care device. There was also no difference in accuracy when we analyzed subpopulations such as subjects with common morbidities like diabetes or asthma, or in healthy subjects. Smoking, which often correlates with elevated hemoglobin levels, did not affect the accuracy of the noninvasive measurement, but medium to dark pigmentation, which has been shown to affect SpO2 accuracy in some studies [18], was shown to increase bias.

Some may ask whether the accuracy of either noninvasive or invasive point-of-care devices allows them to replace venous sample testing and laboratory analyzer analysis. We believe that some point-of-care test values will continue to require additional confirmation, like many point-of-care tests. In our opinion, any reduction in accuracy is more than offset by the value of hemoglobin assessment during the patient encounter, with the potential for more efficient and effective health care. Based on the accuracy observed in this study and other studies, SpHb may be able to be used to effectively screen a significant portion of the population for anemia. Data published by the Centers for Disease Control show that the mean hemoglobin concentration in the US is 13.9 ± 1.5 g/dL [19]. With an accuracy of ± 2 g/dL 95% of the time (2 SD) and with a threshold for treatment for anemia at 9.5 to 11 g/dL, SpHb could be used to safety screen between 73 and 95% of the population to rule out anemia (SpHb values of ≥11.5–13 g/dL) and an additional 0.5% of the population to rule in anemia (SpHb values of 7.5 – ≤10 g/dL). It is important to note that the standard method of screening anemia in many health settings, point-of-care devices such as HemoCue, has similar accuracy to noninvasive testing but requires an invasive capillary sample.

Our study is limited by its lack of a large number of all relevant patient types. Additional studies may demonstrate different results in other patient populations.

We also did not analyze venous blood samples using the international standard for hemoglobin testing, HiCN, so we were unable to evaluate the accuracy of our chosen reference method, the hematology analyzer.

In conclusion, our study shows that noninvasive hemoglobin measurement with SpHb offers similar accuracy as another established point-of-care method (HemoCue) in an outpatient clinic environment. Its noninvasive and quick testing characteristics may translate into added benefits to patient care.

ACKNOWLEDGEMENTS AND SOURCES OF SUPPORT

The authors acknowledge Masimo Corp. for assistance with protocol development, data analysis, and technical review of the manuscript.

NS is Speaker Board Member and Advisory Board Member of Masimo Corp. EAO and GJM received financial support from Masimo Corp for the conduct of the study. Masimo provided the equipment on loan for the study.

REFERENCES

1. Steindel SJ, Rauch WJ, Simon MK, Handsfield J. National Inventory of Clinical Laboratory Testing Services (NICLTS). Development and test distribution for 1996. Arch Pathol Lab Med 2000;124:1201–8.
2. Berkow L, Rotolo S, Mirski E. Continuous noninvasive hemoglobin monitoring during complex spine surgery. Anesth Analg 2011;113:1396–402.
3. Causey MW, Miller S, Foster A, Beekley A, Zenger D, Martin M. Validation of noninvasive hemoglobin measurements using the Masimo Radical-7 SpHb Station. Am J Surg 2011;201:590–6.
4. Frasca D, Dahyot-Fizelier C, Catherine K, Levrat Q, Debaene B, Mimoz O. Accuracy of a continuous noninvasive hemoglobin monitor in intensive care unit patients. Crit Care Med 2011;39:2277–82.
5. Massey D, Martin JA. The New Immigrant Survey (NIS) skin color scale: Office of Population Research, Princeton University; Princeton, NJ; 2003.
6. Procedures for the handling and processing of blood specimens for common laboratory tests; Approved guidelines, 4th edn. Wayne: Clinical and Laboratory Standards Institute; 2010
7. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307–10.
8. Top 100 lab Procedures, Medicare Part B Physicians/Supplier National Data - CY 2007. In: Centers for Medicare and Medicaid Services, editor.: CMS.gov; 2007.
9. Gayat E, Aulagnier J, Matthieu E, Boisson M, Fischler M. Non-invasive measurement of hemoglobin: assessment of two different point-of-care technologies. PLoS ONE 2012;7:e30065.
10. Administration Implements New Health Reform Provision to Improve Care Quality, Lower Costs Fact Sheet. [Web page]: U.S. Department of Health & Human Services; 2011 [updated 2011; cited 2012 5/14/2012]; Fact Sheet]. Available from: http://www.healthcare.gov/news/factsheets/2011/04/valuebasedpurchasing04292011a.html.
11. Armstrong E, Joutsi-Korhonen L, Lassila R. Interaction between clinic and laboratory. Thromb Res 2011;127(Suppl. 2):S2–4.
12. Berkow L. Factors affecting hemoglobin measurement. J Clin Monit Comput 2013. [Epub ahead of print]
13. Recommendations for reference method for haemoglobinometry in human blood (ICSH standard 1986) and specifications for international haemiglobincyanide reference preparation (3rd edn). International Committee for Standardization in Haematology; Expert Panel on Haemoglobinometry. Clin Lab Haematol 1987;9:73–9.
14. Gehring H, Hornberger C, Dibbelt L, Rothsigkeit A, Gerlach K, Schumacher J, *et al.* Accuracy of point-of-care-testing (POCT) for determining hemoglobin concentrations. Acta Anaesthesiol Scand 2002;46:980–6.
15. Gehring H, Duembgen L, Peterlein M, Hagelberg S, Dibbelt L. Hemoximetry as the "gold standard"? Error assessment based on differences among identical blood gas analyzer devices of five manufacturers. Anesth Analg 2007;105(Suppl.6):S24–30.
16. Lamhaut L, Apriotesei R, Combes X, Lejay M, Carli P, Vivien B. Comparison of the accuracy of noninvasive hemoglobin monitoring by spectrophotometry (SpHb) and HemoCue(R) with automated laboratory hemoglobin measurement. Anesthesiology 2011;115:548–54.
17. Raikhel M. Accuracy of noninvasive and invasive point-of-care total blood hemoglobin measurement in an outpatient setting. Postgrad Med 2012;124:250–5.
18. Feiner JR, Severinghaus JW, Bickler PE. Dark skin decreases the accuracy of pulse oximeters at low oxygen saturation: the effects of oximeter probe type and gender. Anesth Analg 2007;105(Suppl. 6):S18–23.
19. Hollowell JG, van Assendelft OW, Gunter EW, Lewis BG, Najjar M, Pfeiffer C. Hematological and iron-related analytes–reference data for persons aged 1 year and over: United States, 1988–94. Vital Health Stat 11. 2005;(247):1–156.

